OBSERVATIONS

on the

STURGE-WEBER SYNDROME

by

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CONTENTS.

In this Thesis some original observations concerning the Sturge Weber syndrome will be placed on record, and new deductions therefrom and from the literature will be submitted.

A survey of the literature reveals that many cases described as examples of the Sturge Weber syndrome can hardly be accepted as such; some are cases of intracerebral racemose angioma, some of the patients have a facial naevus but scanty neurological symptoms or deficits are recorded; a few lack the facial cutaneous stigma. A rather rigid definition of the Sturge Weber syndrome seems therefore justifiable and desirable.

The Sturge Weber syndrome is characterised by cutaneous angiomatosis (capillary naevus, naevus flammeus) affecting the face, epilepsy, gyriform calcifications within the cerebral cortex in relation to an angiomatosis at leptomeningeal level, and in many cases, buphthalmos or glaucoma. The intracerebral calcifications are not visible radiologically at birth. When the lower part of the face is included in the naevoid area the soft tissues of the face, notably the lips and the buccal and alveolar mucosa, are often hypertrophied.

HISTORICAL SURVEY.

Although priority in the literature is claimed for Schirmer (1860) particularly among ophthalmological writers, his case lacked several essentials of the syndrome and was reported with no mention of neurological symptoms or signs. Sturge deserves credit for maintaining, against opposition, it is said, that the epilepsy in a case which he showed before a meeting of the Clinical Society of London in 1879 was probably due to a naevoid condition of the brain akin to that of the patient's face.

William Allen Sturge, M.V.O., M.D., M.R.C.P., was born in 1850 in Bristol (the city of the writer's adoption). He began his studies at the Bristol Medical School and completed them at University College Hospital. He was a registrar at the National Hospital for the Paralysed & Epileptic and later studied under Charcot and Fournier. He was appointed to the staff of the Royal Free Hospital. In his later years he acquired fame as an archaeologist. He died in 1919.

Kalischer (1897) was presented with the opportunity of verifying at post mortem that Sturge's surmise had been correct.

F.Parkes Weber (1922) first drew attention to the "festooned" calcifications apparent radiologically within the cranial cavity. In Scandinavia priority is claimed for Wissing who demonstrated typical skiagrams a year earlier at a radiological meeting in Copenhagen, but his observations were not published until 1929 (with Krabbe).

It had been assumed that the calcifications so characteristic of the anomaly lay in the abnormal vessels at the surface of the brain. Krabbe (1934) is given credit for showing that the calcifications are intracortical. In fact, as has been pointed out by van Bogaert (1950), as far back as 1912 Volland had given a clear description of the calcifications in a case which is fully acceptable as an example of the Sturge Weber anomaly: his paper appeared in a journal now of very limited availability, which probably accounts for its having been overlooked.

Kalischer's patient was too young to have shown any conspicuous degree of calcification, but it is curious that there was no pericapillary calcification in this case.

The name of Dimitri (1923) appears in some papers, linked with those of earlier authors, in token of his description, in a South American journal, of the intracranial calcifications soon after that of Parkes Weber.

In recent years the terms encephalo-trigeminal or encephalo-facial angiomatosis have been proposed. Neither is quite accurately descriptive because the cutaneous manifestations often overstep these areas in the recorded cases. Later in this Thesis it will be submitted that the apparent relationship of the naevus to the

distribution of trigeminal branches is merely fortuitous. It has to be noted however that the involvement of the face by the naevus, and indeed of one particular part of the face as will be seen later, is an essential part of the syndrome. Dr. Parkes Weber (1954) has recently declared in favour of encephalo-facial angiomatosis as an appropriate style for the condition which bears his name, though he comments on the frequency with which the naevus extends beyond the limits of the face.

In this Thesis the term Sturge-Weber syndrome will be retained. Eponyms have been expunged from anatomy; but in clinical matters the sentiment of commemorating astute observers may be condoned, and even encouraged if precision be aided thereby. The Argyll-Robertson pupil is one example. Sir Henry Cohen has aptly described eponyms as a conceptual shorthand (R.S.M. discussion, February 1955). The names of Sturge and of Weber have for so long been in customary usage, and with justification, that they can reasonably be perpetuated. Olivecrona, in his monograph with Bergstrand and Tonnis (1936), expresses the same opinion.

GENERAL COMMENT

The material on which this Thesis is based consists of seven clinical cases. Deductions are made, deriving from the distribution of the naevus in the personal and recorded cases. Observations have been made at operation in five of the cases relating to the circulation within the abnormal blood vessels on the surface of the brain. The records of the electrical activity of the exposed brain are remarkable, unexpected, and informative.

The chemistry of the cortical deposits has been investigated anew (by a colleague).

Earlier accounts of the value of lobectomy in assisting control of the epilepsy have been corroborated. A special significance is thought to attach to the early history in some of the cases, with reference to epilepsy and intellectual retardation.

Each of these topics is in this Thesis a subject-heading relating to all or most of the personal cases studied, and it is therefore proposed to deal with these matters consecutively as revealed in the cases, rather than to detail fully each case in series. The case-records will, however, first be presented formally, but with abbreviation where particular findings are later to be collated and discussed.

CASE I

KNIGHT, Patricia: aged 14 years (in 1950)

No relevant familial abnormalities and no left handedness. A unilateral facial naevus was apparent at birth.

First attack of unconsciousness was at the age of 13 months, and there were no convulsions: she remained deeply somnolent for two days then "wakened" apparently normal. Brief attacks of left hemiparesis began soon afterwards, without twitching or loss of consciousness, and recurred every two weeks or so until the age of five years, when this type of attack ceased.

After an interval of a year petit mal attacks appeared, usually singly, at intervals of a month or so. From then on she was given phenobarbitone regularly up to the time she was first seen, at the age of 14 years. The attacks had gradually become worse and for 18 months she had been unconscious for about five minutes in the majority of the attacks but had exhibited no twitching and had never voided urine in them.

For a number of years she had been liable to periodical attacks of bad temper, lasting for an hour or more, in which she would be restless and would have violent and destructive outbursts if at all frustrated or opposed.

The "fits" were less frequent when the

attacks of temper were prominent. She had no headaches.

Menstruation began at 13½ years but ceased after two months.

Examination showed a naevus flammeus on the right side involving the forehead, temple, upper eyelid, margin of lower eyelid and the side of the nose. (Fig.1). The naevus was of a rosy purple hue and devoid of irregularities or excrescences on its surface - as in all the naevi in the following personal cases.

Fig.1.

The patient was of average development. B.P. 120/70 mm. The left hand was slightly the

smaller and the left calf was reduced by 1 cm. in girth. The circulation in the limbs was symmetrical.

Right handed. No intracranial bruit. The sclerotic of the right eye showed a faint pink suffusion, resolved with a lens into a multitude of minute tortuous venules. No buphthalmos or glaucoma. The optic discs were normal, but a short distance lateral to the right disc a few rather tortuous venules were to be seen, of normal colour. Visual acuity: J1 right; J2 left. Complete left homonymous hemianopia with probable bisection of macular vision. Apart from a slight supranuclear left facial paresis, cranial nerve functions were otherwise normal.

The only further motor abnormality was an increase in the left supinator reflex. No apraxia. Co-operation in tests for sensory functions was limited: some impairment of joint sense in the left hand was established, and so disproportionately gross an astereognosis that this was nevertheless included in the positive findings. Abdominal reflexes symmetrical.

Intellectually this gauche and shy girl was retarded. Her Wechsler scale performance scores were: verbal I.Q. 55; full scale 52. Performance I.Q. 58. Description, "feeble minded". On the Ravens matrices her raw score was 23 and her percentile rank 5. Grade V, intellectually

defective. With Porteous mazes she was successful to year 8. Her Rorschach performance showed several signs characteristic of organic cerebral disease: poverty of output, perseveration of ideas with successive cards, then a sudden change to another persisting idea.

Fig.2

The radiological appearance is shown in Figs. 2 and 3. The long extension of double-contoured calcification into the right temporal lobe in this case is to be noted. The impression created by the disposition of the calcifications is one of marked cerebral shrinkage away from the skull, yet at operation in this and subsequent cases no subdural effusion was encountered, and with one exception the subarachnoid space contained no

excess of fluid.

Fig.3

Arteriography, 1.4.50. The common carotid artery was injected on each side and stereoscopic views were taken. On the normal side good filling of arteries supplying the occipital lobe was obtained, whereas on the right side the filling posteriorly was poor. The films were exposed at comparable phases after injection. The venograms showed a good array of parieto-occipital superior cerebral veins on the normal side, but none in that region on the abnormal side. Instead, a large vein coursed between upper Rolandic and Sylvian regions.

There matters rested for a year. She was at

a special school for epileptic children. On gr.iv. of phenobarbitone daily she was having two minor fits daily, and one major attack monthly. Her behaviour and low I.Q. rendered her unacceptable for later reception into a colony, and the special school refused to accept her back after holidays. An impasse had been reached.

The situation was reviewed in the light of the beneficial results which were then being reported after hemispherectomy in selected cases of epilepsy with hemiplegia. It was felt that a fairly extensive resection posteriorly would not be likely to add much deficit in view of the hemianopia and astereognosis. At first it was thought this was a pioneering venture in Bristol but subsequent reference to the monograph showed that Olivecrona (1936) had performed lobectomy with benefit in several cases of the Sturge Weber syndrome.

Electro-encephalography before operation (W.Grey Walter, Sc.D.) gave a "surprising result", revealing a region of electrical inactivity from the right occipito temporal channels. A large voltage focal persistent slow discharge came from the left temporal lobe, with obvious delta and theta components. A toposcopic survey confirmed the inactivity over the diseased area. (This tracing will be figured later, in the section on Electro-encephalography).

OPERATION, 16.11.51. Occipito-parieto-temporal lobectomy, right side. Electrocorticography. Anaesthesia: cyclopropane and oxygen. Pentothal and ether avoided because of the observations planned.

The scalp was rather more vascular than normal, of a degree common in cases of meningioma. A large bone flap was raised. The dura was normal, and there was no subdural fluid.

The exposed brain was found to be completely obscured over a wide area by a close network consisting of a multitude of tortuous venules of rather even calibre and about 1 mm. in diameter. This formation concealed the entire occipital, and most of the parietal, lobes; only the superior temporal gyrus was not obscured at that part of the temporal convexity exposed in the operation field.

The abnormal venules of the angiomatose areas were of a darker blue than the normal veins elsewhere. There was no vascular engorgement. The angiomatose area was fairly sharply delimited anteriorly; in general the transitional zone to "normal" subarachnoid space and cortex was not wider than 5-8 mm. The arachnoid of the angiomatose areas, and wide of it for 1-2 cm. was opaque and thickened.

The angiomatose part of the brain was much firmer than normal, and the gyri in many places

were somewhat atrophic. On palpation there was no "step" at the transition to brain of normal consistence, to indicate any substantial shrinkage of the sclerosed brain tissue.

The appearance at operation is shown in Fig.4.

Electrocorticography, which will be illustrated and discussed later, revealed almost complete electrical inactivity over all the angiomatose areas, and gross dysrhythmia in the cortex of normal appearance.

Resection of brain was commenced just behind the post-central gyrus, in places superiorly including part of this gyrus where the vascular anomaly extended on to it. The line of resection extended downwards and forwards sparing the lower half of the post-central, and the superior temporal, gyri. The anterior half of the temporal lobe was left in situ, and in cutting through it gritty calcified tissue was evident at the lateral and inferior surfaces of the lobe.

Superiorly the plane of resection was perpendicular to the median plane, then it inclined in a posterior direction to reach the falx almost at the posterior limit of the tentorial aperture. The resection passed lateral to the body of the lateral ventricle for the most part but included the posterior horn and opened the posterior half of the temporal horn.

There was no haemorrhage of note, and none

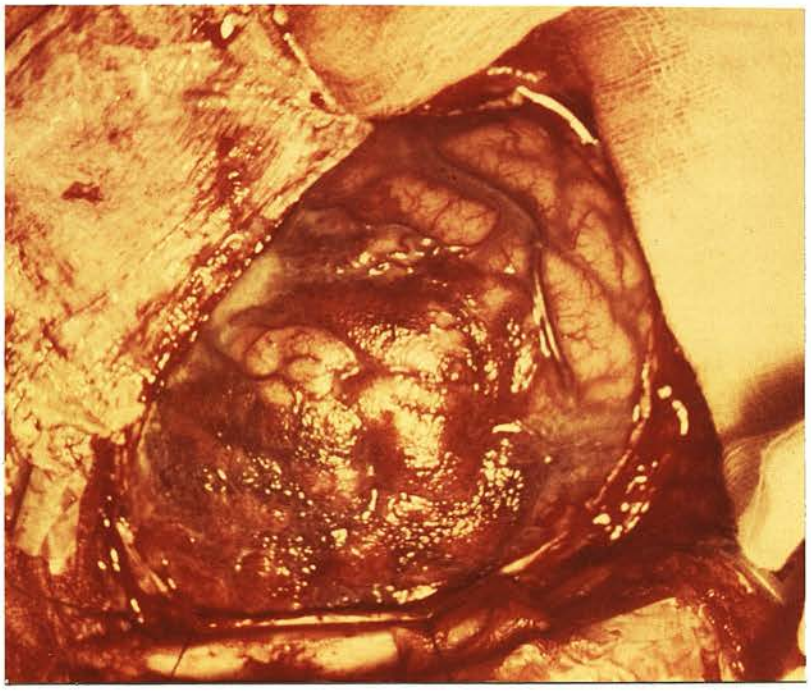


Fig. 4a.

Fig. 4b.

from the calcified brain where it was cut through inferiorly.

Silver clips in pairs were applied to the margin of the resection at the convexity (in addition to others necessitated to control larger veins). Four such pairs of markers can be seen in Fig.5 from a film taken four years after operation.

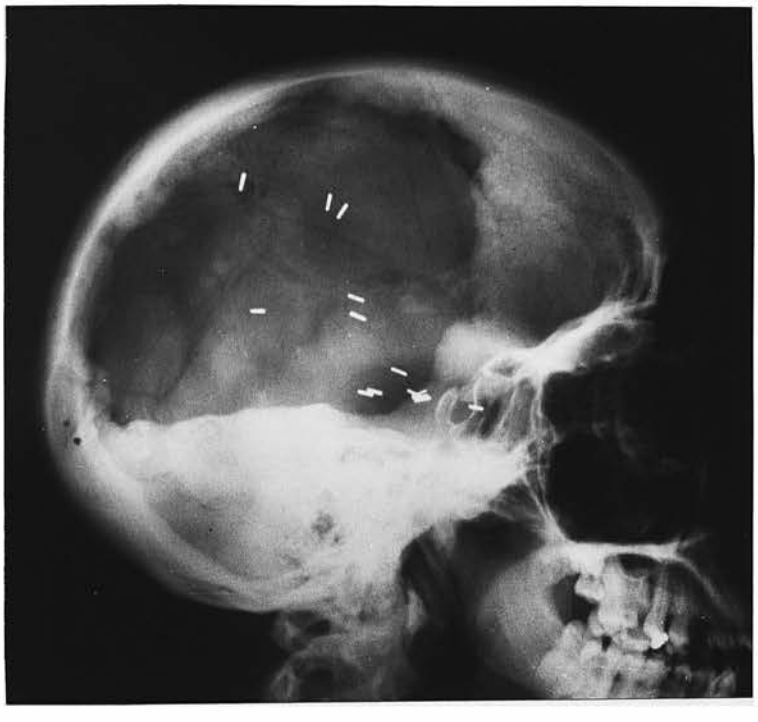


Fig.5

The patient recovered with a left hemiplegia, motor recovery commencing in the lower limb after five days, and at the left shoulder in ten days. The hand and wrist remained completely paralysed and spastic. Gross loss of proprioceptive sensation in the limbs on left side, with some recovery in the lower limb in the ensuing year.

An operative infection necessitated removal of the bone flap five weeks after operation, and by choice it has not been replaced. Plaques of ossification are appearing in the craniectomy gap.

The post operative history with regard to epilepsy is noteworthy. One generalised major attack occurred on the fifteenth post-operative day and phenobarbitone was recommenced, gr.i. b.d. A single major convulsive attack occurred nearly a month after operation, and five days after the wound infection was discovered. In this attack the paresed left side of the face and left upper limb were first involved, and before the attack was over, in two minutes, lesser convulsive movements affected the left lower limb, then spread to the lower limb and trunk on the right side. The head was turned to the left; the upper limb and face on the right side were not involved. Consciousness seemed to be retained throughout the attack. Phenobarbitone was increased to gr.iii. per diem, with Epanutin gr.iss., b.d.

The later history is one of progressive disappearance of the epilepsy, with gradual withdrawal of anticonvulsant drugs until they were stopped one and a half years after lobectomy.

When the patient was last seen in September 1957 (aged 21), the freedom from epilepsy was continuing, without drugs. No temperamental lability.

Progressive improvement in practical capacity was reported, and she had been in paid part-time employment as a home-help for seven months. Her left hand remains useless, though spasticity has lessened: resumption of wearing of a cock-up splint and a course of physiotherapy again is likely to restore some function to this hand. Her reading and writing performance is that of about age ten years: she attends reading classes at a special school.

Her shyness is less and self confidence much improved. Perhaps the successful obscuring of her facial naevus with make-up has contributed thereto,

It has been suggested by Iannuccelli (1949) from studies of skin temperatures on exposure, and sweating, that the naevoid area behaves like skin in a sympathectomised area. Sweating tests are planned shortly but on the evidence from Cases III and IV., are unlikely to show anidrosis. Opportunity will be taken also to check the ocular tensions, because the optic cup on the side of the naevus is now rather deeper and paler than its fellow, although the globe does not feel glaucomatous.

Recent electroencephalographic examination showed some low amplitude delta and theta activity from the right temporal region but no strikingly abnormal discharges were recorded.

CASE II

HIRE, Rita: aged 8 years (in 1953)

No familial left-handedness.

Born with a naevus flammeus on the left side of the face. The only point of note in her early history is that she began to talk at the age of 3 years.

At the age of 3 years she had her first epileptic attacks, initiated by convulsions of the right side of the face as she lost consciousness. At that stage in the attacks, which were stereotyped, clutching movements of the flexed right upper limb began, and the right lower limb "kicked out" repeatedly. In some attacks the convulsive movements spread to the limbs on the left side and were often then altogether more violent. Most of the fits were nocturnal. They came in groups, and could last for a week - day and night, every hour or so. Long remissions were known, not exceeding three months. She was never incontinent.

Some improvement in the epilepsy followed increase of phenobarbitone to gr.ii.daily.

When she was older she was able to describe an aura of a "crawling" paraesthesia in the epigastrium.

She had shown left hand dominance from infancy, but used her right hand for some skills, in particular for pitching a ball and for dice-

throwing.

Although backward at school she was said to be with her contemporaries in age.

No headaches. She was equable in temperament on the whole, but she usually retaliated viciously when punished.

Examination showed a freckled child with the naevus flammeus illustrated in Fig.6.

Fig.6

The potential significance of the naevus on the upper lip stopping short at the philtrum was not then appreciated. This paramedian limit of the naevus was carried round on to the buccal aspect of the lip, but on the gum it extended to

the midline. The alveolar arch was malformed to the left of the midline, the curve being flattened anteriorly. The alveolar mucosa was slightly hypertrophied, the central incisors were mal-erupted and of varying degrees of projection. The lower gum and teeth, and the tongue, were normal. The palate, which was highly arched, and the lingual aspect of the upper gum, were also unaffected.

General examination revealed nothing of note. She had a "vacant" unintelligent expression, and the facies of a mouth-breather. The adenoids were large. Her hands were symmetrical in size, and the limbs were also symmetrical in length and girth.

Neurological examination disclosed the

following abnormalities: complete right homonymous hemianopia, probably with bisection of macular vision; right facial paresis of supra-nuclear type; slight loss of power in right grip and of all movements at right ankle and toes. Paradoxically the tendon reflexes of the limbs on the left side were brisker than on the right side. The plantar reflexes were extensor on both sides. The abdominal reflexes were symmetrical.

The surface of the eyeball and the retina exhibited no vascular anomaly.

Radiological examination revealed the characteristic double-contoured gyral pattern of calcification localised to the left occipital lobe in approximately its posterior half, including the pole, (Figs.7 and 8). Some cranial asymmetry is also apparent in antero-posterior view.

When she was admitted to hospital it became evident that she had no recollection of her attacks, and denied their occurrence.

Electro-encephalography before operation (W.Grey Walter, Sc.D.): "On the left side no abnormal rhythms were seen, only very widespread complex slow activity. Occasionally brief abnormal wave-complexes appeared and sometimes spread to the right side, where they interrupted the normal alpha rhythms. The flicker test gave

Fig. 7.

Fig. 8.

a small following response on the right, but none on the left side. The findings suggest marked abnormality of the whole of the left hemisphere".

It is to be noted that no electrically dormant area was found in this case.

OPERATION, 1.7.53. Occipital lobectomy, left side. Cyclopropane and oxygen anaesthesia.

Craniotomy revealed a normal dura. The scalp and bone were of normal vascularity. On opening the dura the characteristic Sturge Weber type of meningeal angiomatosis was exposed. The dense carpet of small tortuous venules of even calibre completely obscured the cortex over an area extending forwards from the occipital pole for between 5 and 6 cm., measured along the supero-medial and infero-lateral borders of the hemisphere. The anterior limit of the angiomatose area extended roughly in a curve radial to the pole between those two points and was rather sharply delimited except superiorly, where a small area of more open texture of venous tortuosities extended on to adjacent gyri.

The abnormal venules were remarkably cyanosed and this was observable evenly throughout the pathological area. The photographs (Figs.9a and b) were taken with the patient receiving 96% of oxygen for the purpose of the photographs; this had no effect on the reduced state of the blood in the venules.

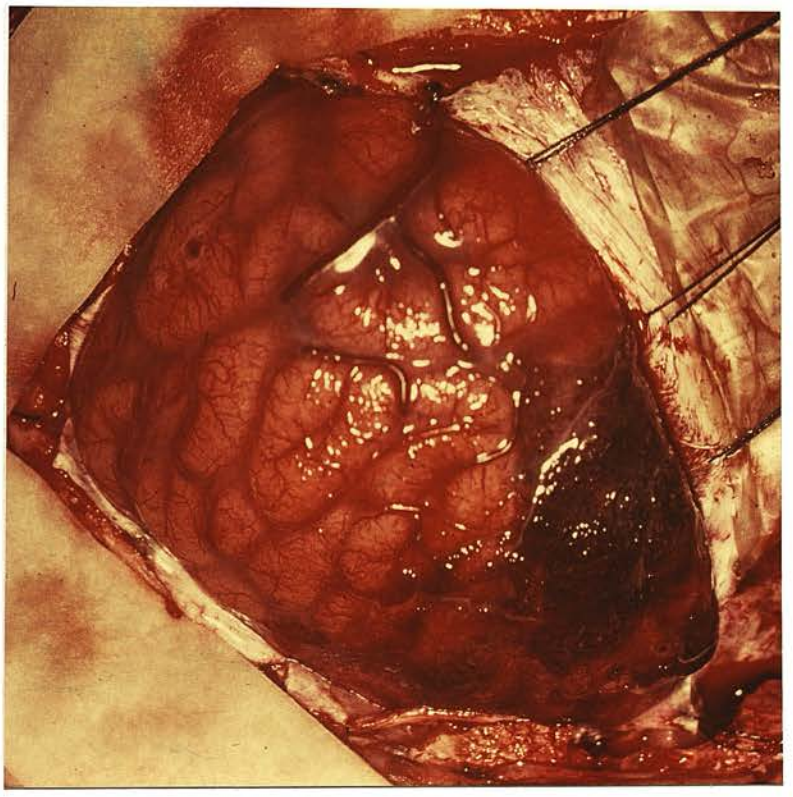


Fig. 9a.

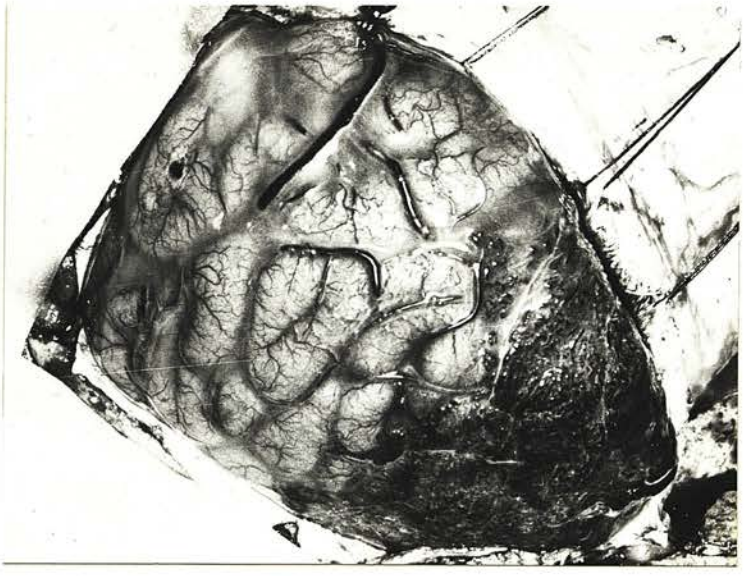


Fig. 9b.

The arachnoid was thickened and rather opaque in many places in the angiomatose area, and this condition extended widely forwards on the adjacent cerebral surface. Here and there gyri in the clear anterior part of the operation field showed slight focal atrophy without palpable sclerosis.

The electrocorticography will be described later.

The lobectomy presented no technical difficulty, and bleeding was minimal. It was found that diathermy coagulation applied anywhere on the surface of the angiomatose area immediately produced the usual blanched area of coagulation without any tendency for the vessels to rupture and bleed.

The plane of resection was carried through almost perpendicularly to the falx, corresponding to a radius of about 10 cm., measured forwards on the convexity from the occipital pole. No important cerebral vein was sacrificed. To the naked eye the cut surface of the hemisphere appeared normal. The angiomatose area covered the medial surface of the occipital lobe, but was rather patchy in distribution inferiorly.

It had been hoped to record the electro-encephalogram from the frontal scalp immediately after the lobectomy, but the presence of wet

towelling over the electrodes vitiated useful recording. At the conclusion when the drapes had been removed the recordings became satisfactory. Delta rhythms observed at first could have been due to anaesthesia but within two minutes the records approached normal. However a burst of abnormal activity heralded a clinical fit of her usual pattern, just as she was regaining consciousness.

There were no more epileptic attacks until the sixth day when frequent twitchings of the facial muscles on the right side were observed, with no loss of consciousness. These ceased after injection of an anticonvulsant. This was the last epileptic manifestation up to the time of discharge 25 days after operation. She had been given Epanutin gr.iss. and phenobarbitone gr.ss., each b.d.

On recovery from the operation the right facial weakness was still evident, for a week rather worse than previously. There was no paresis elsewhere and tendon and other reflexes were normal. Depression of joint sense in the fingers was slight and only a few errors were made in stereognostic tests with the right hand.

She was seen again about a year later. Four probable nocturnal attacks had occurred but none were witnessed because they were now of short

duration. All took place soon after retiring to bed. She had been receiving phenobarbitone alone, gr.ss. b.d., for the five months before she was seen and one of the probable attacks had occurred in that period.

She had become much more helpful in the house and had shown improved application to other tasks. Her headmaster reported that no improvement in her scholastic ability had been observed, and she was becoming more vicious towards other children. Her parents commented that she was known in the school as "Redface" and was often taunted about her appearance. The facial paresis, present before operation, had disappeared. The sensory state of the right upper limb remained unchanged. She was much less distractable at interview than before operation. Her scholastic ability was assessed by her teachers as roughly that of a child three years her junior.

This patient was reviewed in September 1957, (four years after lobectomy), and continued slow improvement in ability and temperament was reported. Only two very short epileptic attacks had occurred on successive nights a year previously, with no incontinence. The best anticonvulsant medication has been found to be phenobarbitone one and a half grain and Mysoline three grains per day.

Recent reports from school indicate that in

arithmetic, comprehension and word recognition her age is 6 - 8½ years: in spelling it is only 5½ years. She is at times spiteful and quarrelsome at school, exhibiting a delight in "bossing" others. The teachers have difficult phases with her but she usually becomes amenable. Obviously she is a problem child at school, but not at home where her mother dominates her wisely.

Electroencephalograms at intervals have shown a temporal focus on the dominant side, ipsilateral to the naevus.

The only new feature on examination is a hypertrophy of the naevoid upper alveolar mucosa and increased irregularity there of the teeth. The bony alveolus has also increased in length and interdental spaces are evident. Motor and sensory functions in the limbs are satisfactory. The limbs have developed symmetrically.

Although overt epilepsy is under control this child's troubles at school may well be related to the discharging left temporal lobe. Her scholastic progress has been disappointing and it is questionable if the lobectomy has been of any direct benefit in that direction, though perhaps the progressive deterioration so often reported during school years has been avoided in this case.

CASE III

RICKETTS, Gerald: aged 14 years (in 1950).

The personal and family history contained nothing of note except that the patient was one month premature at birth and weighed 5 lbs. Labour uneventful. Born with a naevus on the right side of the face.

The first epileptic attack occurred at the age of 3 months. From the start these were of focal type, commencing with convulsive movements of the left upper limb, and followed by rigidity of all limbs and of the body. Consciousness was sometimes lost, and urine was voided on most occasions. In addition he had regular nocturnal enuresis in his early years.

The fits had continued, in general slowly increasing in frequency, and latterly a transient post-ictal paresis of the limbs on the left side had been noted. He had been receiving a moderate dose of phenobarbitone since the age of 3 years but this had been gradually increased to 4 grains daily in spite of which attacks would occur on the slightest excitement, and spontaneously in frequent groups of three or four. These more recent attacks were ushered in by tonic flexion of the left upper limb which then jerked slowly into an extended position as the face began to twitch on the left side. At that stage of the

fit he often tried to speak through clenched teeth as the lower limbs became rigidly extended. At that point he always lost consciousness, and the attack terminated with clonic movements of the limbs on the left side.

He was generally irritable and more obtuse mentally for a day before each episode. Latterly, incontinence in attacks was infrequent, and post-ictal weakness of the limbs had ceased.

The milestones of infancy were passed rather later than normal. His intellectual development was grossly retarded and his later education consisted largely of handwork, at which he was very slow in acquiring any modest degree of proficiency. His reading standard when he was 18 years old was about that of a child of 8 years. His verbal performance and intelligence quotients were 53 and 54; full-scale 47. The Rorschach test gave a mental defective pattern. He was well down in the mental defective range on the Bellevue-Wechsler intelligence scale. His performance on the Bender-Motor-Gestalt corresponded to the age of 8 - 9 years. His drawing ability was good. His spelling was elementary. He was incapable of writing down figures containing more than two digits.

Fig.10

The right side of the face showed the naevus flammeus illustrated in Fig.10. The vasculature of the sclerotic and of the retina was not increased. There was no intracranial bruit. The teeth and palate were normal.

In appearance he was a rather lanky youth, but well developed. The secondary sexual characteristics were normal. The limbs were symmetrically developed.

In cranial nerve functions the only abnormality was a slight left facial paresis of supranuclear type; in particular the visual acuity, and the fields for white and colour were full (2/330, 2/2000 white: 10/2000 red).

Motor functions showed a reduction in power in most of the muscle groups in the left lower

limb to between 60% and 70% of normal, the left knee and ankle jerks were increased and the plantar reflex was extensor. He walked with a slight limp and a tendency to inversion of the left ankle at each step. The left upper limb was normal. The left abdominal reflexes were depressed.

The sensory deficiencies consisted of gross loss of joint sense up to and including the left elbow, but joint sense was normal in the other limbs. Two point discrimination -20% of errors with the left hand. Graphaesthesia -50% of errors with the left hand but there was an occasional error with the other limbs and the performance was obviously impaired by his scholastic shortcomings. Stereognosis was good in both hands. Vibration sense preserved.

Radiological examination of the skull (1954) showed rather widely scattered faint calcifications high in the posterior parietal region, stopping at the approximate level of the parieto-occipital fissure. Only one of these shadows delineated by double-contouring a short stretch of cerebral sulcus. In the antero-posterior view the shadows were barely discernible, on the right side: marked cranial asymmetry was apparent. By good fortune a lateral view taken four years earlier (when he was 14 years old) was available for comparison, and there was no doubt that the calcific shadows

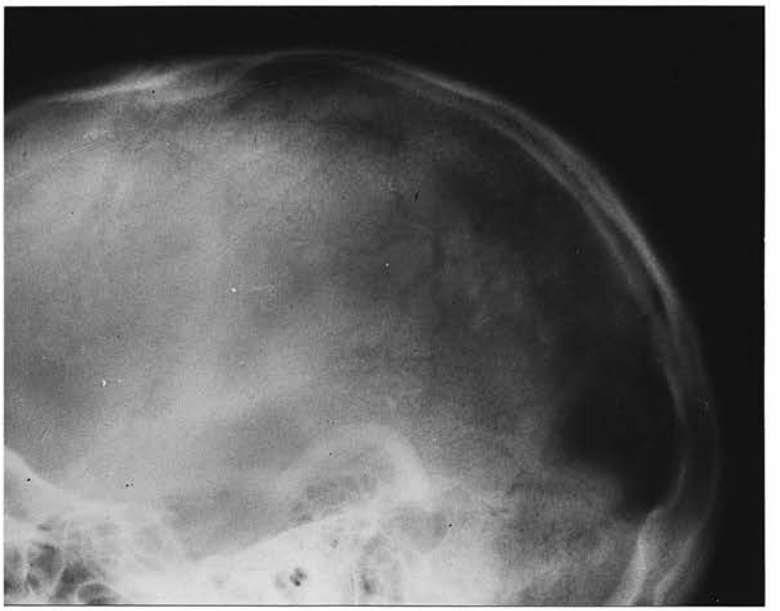


Fig. 11a.

Fig. 11b.

had acquired some substance in the interval.

Arteriography 1950, by exposure of, and injection into, the right internal carotid artery showed no paucity of parietal arterial filling, and the films were considered normal.

The experience with the previous two cases prompted consideration of lobectomy in this case and with the concurrence of a neurosurgical colleague, Mr.D.G.Phillips, under whose care the patient had been so far, operation was proposed.

Electro-encephalography.

A report of March 1946 (when the patient was 10 years of age) was available. The dominant rhythm was 6-7 c/s., most evident over the vertex on both sides. Secondary peaks at 1½-3 c/s. were detected without focal features. Dr.Grey Walter reviewed the tracings in the light of the experience in Cases I.and II.and found no suggestion of a "silent" area. The records of nine years later, shortly before operation, showed no noteworthy change.

OPERATION 12.5.54. Resection of angiomatose area of cerebral convexity, right parieto-occipital. Anaesthesia: cyclopropane and oxygen.

While a large bone flap, suitably placed, was being raised the scalp and bone were seen to be of normal vascularity. When the dura was reflected

it was found to be lightly adherent at a few places only, over the angiomatose area; its deep surface presented no abnormal vessels.

The angiomatose area in this case extended on the supero-medial border of the hemisphere from a point about 2 cm. above the occipital pole upwards and forwards for 6 cm. From this base a very roughly triangular area of interlacing venules extended over the convexity almost as far as the infero-lateral border. Two small areas with the venules more widely spaced overlay the cortex, the lowest of which was in relation to the middle temporal gyrus. They were almost isolated offshoots from the main angiomatose area.

Fig.12

The venules in the subarachnoid space were so closely-set that the underlying gyri could not be seen, but on tangential inspection the gyral pattern was clearly visible. This feature had not been evident in the previous cases, perhaps because the

venules in this case were of smaller calibre with a lumen which would admit a stout horsehair perhaps. The blood in them was less cyanosed than in the previous cases, and in most of the area the colour approximated that of veins in the unaffected parts of the cerebrum. Two veins of moderate size coursed upwards towards the midline in sulci, and the arachnoid in their immediate vicinity was studded with small calcifications. The arachnoid membrane was moderately opaque in places over the vascular anomaly in its main part. The gyri were not apparently atrophic.

The "lobectomy" took the form of resection of a triangular slab of the convexity, measuring about 7 cm. along each side, including a maximum depth of 3 cm. on the medial surface of the hemisphere. It would have been profitable to have mobilised the supero-medial border at the outset and to have inspected the medial surface, because the angiomatosis was sharply limited at the supero-medial border of the hemisphere. A rather shallower resection would have been permissible. The outlying temporal offshoots of the lesion were not disturbed. Except medially, the brain tissue removed was 1.5 - 2 cm. thick. The consistence of the brain was normal in the planes of section chosen.

Electrocorticography will be described later.

On the evening of operation the left upper

limb was paresed, the strongest movement being flexion of the elbow (about 70% of normal): shoulder movements were most affected. Next morning the limb was immobile except for a trace of finger-flexion. Cutaneous sensation was well preserved but two-point discrimination and graphaesthesia for numerals had vanished. Joint and vibration senses were lost in the distal half of both limbs on the left side. Motor recovery in the upper limb began on the fifth day, by which time the lower limb was well on the way to full recovery. Motor and sensory recovery proceeded at a satisfactory rate up to the time of the patient's discharge nearly three weeks after operation. His gait had returned to its pre-operative state, but a residue of paresis in the upper limb, attributable to the operation, was still present. A lower quadrantopsia, homonymous in the left half-fields, was resolving.

One focal convulsive attack occurred about 24 hours after operation, and phenobarbitone was increased to gr.iii. and Epanutin to gr.ivss.per day. A few days later the phenobarbitone was halved but major attacks followed two days later, without incontinence. Three days before discharge Mysoline 0.75 G.per day was started and no further attacks were seen in hospital.

He was re-admitted six weeks later having had 10 attacks at 30 - 40 minute intervals throughout

the preceding night (on Mysoline only as above). Phenobarbitone gr.ii and Epanutin gr.iii daily were substituted.

In the ensuing four months he had about a dozen attacks, none of which were witnessed at the outset as they were nocturnal. The jactitations were generalised each time he was reached by his parents, the whole attack lasting probably less than a minute. The dose of anti-convulsants had been halved for two months.

Gradually the epileptic tendency diminished and at interview nine months after operation it was learned that only two minor focal attacks had occurred, on phenobarbitone gr.iii. and Mysoline 0.5 G. daily.

The nocturnal enuresis (sic), which had been improving before operation, ceased soon afterwards. Further, he had not been incontinent in the major attacks which had occurred in the early months after operation.

A substantial and progressive improvement in his alertness, independence and purposiveness has been noted. His work at an Industrial Centre shows steady progress. He finds his way there and back, a considerable distance of miles, by public transport and unaccompanied; his hours of work are 8 a.m. to 5 p.m. His memory has much improved and he is trustworthy in errands and in performing tasks in the household. Previously he had been

unable to undertake the simplest tasks without supervision and had to be escorted to and from his special Centre every day.

The patient was reviewed in September 1957. Mild epileptic attacks continue, consisting of a straightening of the trunk and limbs, and groping movements of the outstretched left hand. He seems to retain consciousness and the attack is over in fifteen seconds or so. These episodes occur once every one or two months. He is receiving 0.5 G. of Mysoline and gr. iii. of phenobarbitone daily. There is no incontinence.

Traces of a left hemiparesis remain, and his limping gait is still evident, but the plantar reflexes are flexor. The sensory deficiencies are stationary.

At his special Centre he is considered capable now of trying for some selected paid employment in carpentry.

A sweating test showed a symmetrical outburst of sweat on the face. Ocular tension was normal (18 mm. bilaterally).

Recent electroencephalographic record showed, as at the previous examination a year ago, some low amplitude theta activity from the right parietal area.

CASE IV

EMSON, Irene: aged 9 years.

She is the youngest of three girls, one of whom is of a notably high grade of intelligence. Nothing else of note in family or personal history, apart from a birth mark on the right side of the face.

Infancy was normal up to the age of 11 months: she sat up at six months, was walking before one year and had acquired a vocabulary of about a dozen words, including family names.

At the age of 11 months she suddenly started having twenty or thirty brief epileptic attacks daily; in each of these she would suddenly flex both elbows and fall forward unconscious. She always voided urine. In two minutes she would suddenly recover and at once resume normal activity. In one week she lost all of her vocabulary except "Hallo" which was used often with many other meanings: even this vanished in the next year and a half, during which time she was having fits daily while receiving intermittently a probable bromide mixture. When she was four years of age phenobarbitone in the cautious dosage of gr.$\frac{1}{4}$ b.d. was given for the first time, and that about halved the attacks, each still associated with incontinence of urine.

When she was approaching the age of 5 years she began to have attacks of longer duration, then in addition in some attacks convulsive movements affected the limbs on the left side. Phenobarbitone increased to gr.iss. a day, which stopped the minor attacks, but three or four major attacks a day continued. These convulsive attacks increased in frequency until Mysoline was given.

From the start of the fits at 11 months her ability to hold her head erect began to fail, and a left hemiparesis developed progressively. When 4 years old she was admitted to the Fountain Hospital in London, unable to speak but able to stand and walk unsteadily. She seemed to have no comprehension, had no interest in toys or other environment. She was destructive, and her mental age was estimated at 10 months. She had double incontinence. She was transferred to a special home near Bristol when her parents moved to the district. It was thought that Mysoline was successful in controlling her epilepsy (0.75 G. daily).

Examination showed her to be an idiot, with lolling head, wandering attention, eyes deviating to either side, drooling saliva constantly. She was constantly picking up objects and throwing them to the floor in the manner of an infant.

Every two or three minutes her head would

suddenly drop forward, her breathing deepened and slight flexion-twitchings of the fingers on the left side, then of the fingers on the right side, were to be seen for a few seconds. In 15 to 20 seconds awareness suddenly returned spontaneously, or earlier in response to a loud noise. These recurrent phases were interpreted as epileptic attacks.

She was aphonic, only once uttering a rather guttural "animal" sound during the consultation.

The distribution of her naevus flammeus on the right side of the face is shown in Fig.13.

Fig.13.

The deviation from the midline on the forehead is obvious: the naevus is bounded by the midline at the skin of the upper lip. The lip is not hypertrophied. The naevus extended on to the buccal mucosa and reached the midline on the labial aspect of the gum on the right side, but the lingual gum and hard palate were normal. The upper right incisors were slightly irregular compared with those on the left side.

Slight obesity; (because of her distractibility it was found impossible to persuade her to stand to be weighed or to have height measured). Stature about average. Apart from a sacro-coccygeal dimple general examination revealed no abnormalities.

She was right handed, perhaps under obligation because of the left hemiparesis. (One paternal aunt was said to be left handed).

The optic discs were rather pale: no cupping. Ocular tension symmetrical. Left homonymous hemianopia. Pupils normal. No facial paresis.

Moderate grade left hemiparesis without spasticity, asymmetry of tendon or abdominal reflexes: left plantar response extensor. The left lower limb was externally rotated at the hip in walking.

All that could be established concerning sensory functions was a symmetry of the corneal reflexes and of responses to painful stimuli on the two sides of the body.

Electro-encephalography was attempted without success.

Wassermann and Kahn reactions in blood were negative.

Radiologically, scattered faint intracerebral calcifications were evident in the posterior parietal and anterior occipital regions superiorly on the right side. None of these exhibited a double-contour appearance. In antero-posterior view they lay away from the midline, nearer to the median plane than the convexity of the hemisphere.

In the light of experience with the previous cases some hope was entertained that if the very frequent minor epileptic attacks could be brought under control with the aid of lobectomy, some improvement might result in her manageability in the institution. It seemed rather too optimistic to hope for the return of some simple language ability.

OPERATION: 1.12.55. Occipito-parietal lobectomy, right side.
Anaesthesia: intratracheal nitrous oxide and oxygen followed by light intermittent Pentothal intravenously.

The brain posteriorly was exposed on the right side by a large osteoplastic flap. The scalp and bone were of normal vascularity. The

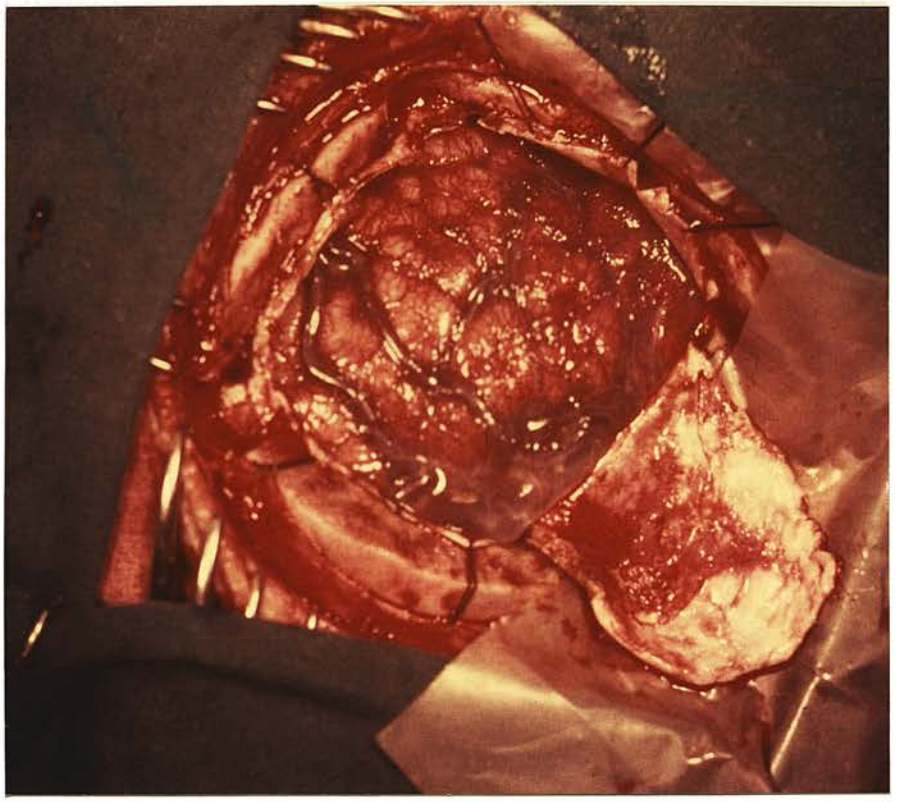


Fig. 14.

dura mater was decidedly more vascular than in the previous cases, resembling the condition common in cases of vascular meningioma, in the vicinity of the tumour. Intracranial tension was normal.

When the dural flap was reflected its deep surface displayed, in a roughly circular area 3 cm. in diameter, a sheet of angiomatose vessels containing rather red venous blood. It was paramedian in situation and centred about 5 cm. upwards and forwards from the occipital pole. This finding in the dura was unique in the personal series of cases. The circulation in those angiomatose dural vessels was restored in about half a second after blanching by pressure. The margins of this dural angiomatose area were not sharply defined and medially the area extended almost to the sagittal sinus.

The cerebral convexity exhibited the characteristic Sturge Weber type of angiomatosis, of a rather more open texture than in the previous cases, except towards the occipital pole, where the vessels completely obscured the cortical surface. The blood in the angiomatose vessels of the more open-textured part anteriorly was not notably cyanotic but towards the occipital pole the colour was decidedly darker than in the cerebral veins wide of the vascular anomaly.

Anteriorly there was no sharp transition from

angiomatose to "normal" cortex, as in the previous cases, the transitional zone extending over about 3 cm. of the surface. The angiomatose area extended over all surfaces of the hemisphere posteriorly, terminating at distances of from 5 to 7 cm. anterior to the pole, measured on the surfaces.

Anterior to the abnormal vascular area the cortex had an entirely normal appearance but was firmer than normal up to the level approximately of the post-central gyrus.

In the upper posterior part of the exposure a large lake of subarachnoid fluid underlay a localised area of marked arachnoidal thickening, close to the sagittal sinus. Two fairly large cerebral veins of normal colour drained downwards and forwards from the region of this lake of fluid towards the lateral sinus. Except at this one place the cortex showed no indication of atrophy.

The plane of lobectomy was approximately coronal, cutting the infero-lateral border at 5 cm. from the pole (measured on the convexity), and at 6 cm. similarly at the supero-medial border. The amputation exposed the vestibule and included the posterior horn. In cutting through the white matter the consistence was everywhere firmer than normal, particularly for the centimetre or two around the lateral ventricle.

The line of resection spared at two points

the anterior limits of the angiomatose area.

The electrocorticograms will be described later.

Several mild epileptic manifestations affecting the limbs and face on the left side were noted in the first two days. Phenobarbitone was replaced by Mysoline (0.75 G. daily), and this was effective for three days. Then twitchings were seen on the right side only of the body: phenobarbitone was progressively substituted for Mysoline. All was well as regards the epilepsy for the next ten days when periodical bouts of twitching reappeared on the left side. Epanutin (gr.iii) was substituted for the Mysoline with improvement. Epileptic manifestations recurred sporadically up to a month after operation and for the two weeks prior to discharge from hospital she was stable on phenobarbitone alone, gr.ss. b.d.

During her post-operative stay of six weeks in hospital the child's awareness of her surroundings improved. She could be fed faster and with less interference from her aimless activity. Her gaze was now more sustainedly held by those handling her. The short periods of head dropping almost ceased and there were no incidents of hyperpnoea and alteration of consciousness. Her gait was improved on its pre-operative state, and she had suffered no set-back in the use of her left upper limb.

This child was readmitted to hospital in August 1957, about eighteen months after operation. She continues free from epilepsy, and nothing has been seen suggestive of the former larval attacks. She has been receiving gr.$\frac{1}{4}$ of phenobarbitone (and advice was given to raise the dosage).

She walks unaided, though not yet normally. Head held erect and attention easily held. She obeys simple commands and can drink unaided if the cup is placed in her hands. She still has to be fed, but eats rather than sucks in food as previously. She behaves in an orderly manner at table. Drooling of saliva is only occasional. She has been continent for a year, with regular post-prandial "servicing". She can give warning of toilet need. Wet clothes and bed are a thing of the past.

About 9 months ago she had a vocabulary of three words, used appropriately, but perhaps because of inadequate phenobarbitone her language retrogressed for a time, but is returning.

The left upper limb has become more useful, and she throws a ball with her left hand. Earlier in the post-operative period she used her right hand, and it would seem that a left hand dominance is asserting itself. She can catch a ball quite well.

The limbs show no spasticity, hyperreflexia or clonus, but the left plantar response is extensor. Her gait shows now no limp.

An epulis between the upper right canine and incisor (on the naevoid side) was removed intact with the adjacent teeth under anaesthesia, without incident from haemorrhage. Opportunity was taken to measure the ocular tensions, and they were normal (15 mm. bilaterally).

A sweating test showed symmetrical appearance of sweat on the forehead, but on the cheek and naevoid half of the lip beads of sweat were about one minute delayed in appearing.

Progressive improvement in this child's capacity is anticipated over the years, and it will be a matter of supreme interest to observe whether her language apparatus can be brought into action after having been in complete abeyance for eight years.

CASE V

WALKEY, Andrew: aged 8 months.

Birth weight 10 lbs. At the age of 5 months he began to have periodical focal convulsive attacks, confined to the left side of the body, lasting for about five minutes, associated with loss of consciousness. These recurred four times in six weeks, and in addition brief attacks of cyanosis and loss of consciousness were noted, sometimes twice in a day. On a small dose of phenobarbitone these disturbances were much lessened.

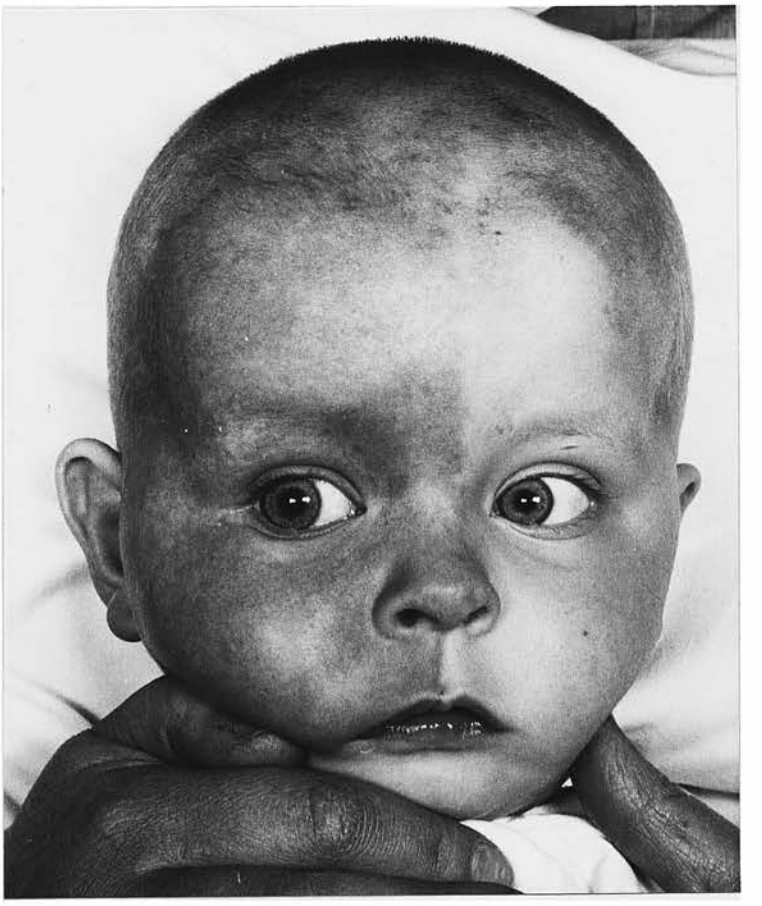


Fig.15

A naevus flammeus was evident on the right side of the face, affecting diffusely the forehead, eyelids, whole of cheek and temple, extending back to the root of the ear, transgressing the midline of the nose, but exactly in the midline of the upper lip. The lower margin of the naevus was not very sharply delimited; it extended down below the level of the mouth towards the angle of the jaw. Patchy extensions of the naevus reached towards the vertex on the scalp. The naevoid state affected the mucosa of the lip and gum, and hard and soft palate, and was bounded by the midline. The dentition was regular and proceeding normally.

The scalp on the left side showed a long oval naevoid patch measuring 7 x 3 cms. to the left of the midline and reaching forward as far as the hair-margin.

The conjunctiva on the right side was slightly reddened, with an excess of fine vessels, but the sclerotics were almost symmetrical in vascularity.

The globe of the right eye was enlarged, and the iris at least 2 mm. greater in diameter. The pupil also was larger on the right, seemingly in conformity with the buphthalmos.

At the midline of the forehead a bony step was visible and palpable, caused by the right half of the frontal bone being either thickened or ante-posed relative to the level of bone on the left of the midline. The bone here was not clearly thickened in standard radiological views of the

skull, and tangential views suggested the prominence to be genuinely due to ante-position of the right half of the calvarium anteriorly. The difference in levels on the two sides was probably no more than 3 mm. at most.

In other respects the infant was well-developed. The face was symmetrical. The maximum girth of the skull was 18½" (47 cm.). Fontanelles normal.

The ocular fundi showed only a pallor of nasal halves of the optic discs. By confrontation test with a coloured light a complete left homonymous hemianopia was readily demonstrated. The limbs moved symmetrically: the plantar responses were still extensor in type.

Four months elapsed before this patient could be admitted to hospital, at the age of 1 year. Only two small focal attacks had been observed in the interval. The infant had not yet attempted to sit up and his vocabulary consisted merely of "Mum", "Dad", and "ta-ta", - rather less than might be expected in this alert, lively and cheerful little person were language functions developing normally. The left upper limb was beginning to lag behind in normal motor activity: tendon reflexes were symmetrical and plantar reflexes now flexor.

The films of the skull still showed no trace of intracranial calcification (stereoscopic views).

Electro-encephalography will be discussed

later.

It was still considered that no good indication for lobectomy had yet appeared. A small craniotomy was made over the occipital convexity on 23.3.56, to prove the existence of the angiomatose state of the meninges and to obtain a biopsy. The exposed gyri were found to be almost completely obscured by a feltwork of venules of fairly uniform size. The blood within was of a reddish-purple colour - certainly not in the least cyanotic. A block about 10 x 15 mm. of whole thickness of cortex was removed for study, without the slightest inconvenience from haemorrhage.

Four days later a series of seizures of his usual type commenced, and it was about half an hour before they were brought under control by drugs. This provided an adequate indication to proceed to lobectomy.

OPERATION: 6.4.56. Occipito-parietal lobectomy, right side.
Anaesthesia: intratracheal nitrous oxide and oxygen with intermittent light Pentothal.

The occipital and a considerable part of the parietal and temporal lobes on the right side was exposed. The soft tissues and dura, but not the bone, were rather more vascular than in the previous, older, cases. The lepto-meninges were

Fig. 16.

seen to be occupied by myriads of minute tortuous venules, covering the occipital lobe from the pole forward for 7 cm., measured along the upper and lower borders of the convexity. At the anterior limit of the angiomatose area superiorly, overlying posterior parietal gyri, there was a tangled leash of veins of the normal blue tint: this area was about 2 x 2 cm. in area. At the infero-lateral border lay a similar arrangement of veins, of about 1.5 x 2 cm. area. Later, when the cerebral resection was being effected, these larger veins were seen to lie entirely in the plane of the leptomeninges. One large vein about 3 mm. in diameter coursed vertically upwards from the anterior limit of the angiomatose area for 4 cm. before disappearing into the brain just forward of the abnormal vascular network. The medial and inferior aspects of the hemisphere posteriorly were covered by the same vascular network as far forward as the posterior limit of the hiatus tentorii, without any larger veins being apparent. Only two superior cerebral and two inferior cerebral veins, all of normal size, drained into the superior sagittal and lateral venous sinuses.

The blood within the network of anomalous venules was not of cyanotic colour. No "arterialised" veins were to be seen.

The lobectomy was commenced along a line corresponding to a radius of 7 cm. from the

occipital pole, coincident for the most part with the anterior limit of the vascular anomaly but including inferiorly a small area (about 1.5 x 1.5 cm.) of cortex of normal appearance. The "plane" of resection extended medially and slightly posteriorly to reach the medial surface at a level about 1 cm. posterior to the free margin of the falx (at its junction with the tentorium). The midbrain showed no abnormal vasculature.

Electrical recordings were made from the surface and from the substance of the occipital lobe, which will be described later.

The immediate effect of this operation was a complete paralysis of the left upper limb, gross paresis of the left lower limb, and slight facial weakness. It was not until the third post-operative day that the upper limb began to show motor recovery.

Convalescence was marred by a staphylococcal (operative) infection manifest by accumulation of infected fluid under the healed scalp flap, but without the clinical picture of meningitis, although the lumbar C.S.F. contained several hundreds of polymorphonuclear cells/c.mm. for a time.

No epileptic disturbances were observed after operation for three weeks, and the operative infection may have played a part in their recurrence at that time, affecting face and arm

on left side only and of Jacksonian type (brief and without loss of consciousness). The bone flap had to be removed at a further operation on 30.4.56, at which evidence of a very indolent infection within the cavity remaining after lobectomy was apparent. After this procedure recovery was fairly rapid. The left upper limb soon returned to its pre-operative nearly-normal activity and all trace of facial weakness vanished.

Occasional twitchings of the left side of the face and of the left upper limb persisted in spite of phenobarbitone gr.$\frac{1}{2}$ b.d. until nearly two months after the lobectomy. During his last two weeks in hospital no twitchings were seen, and the child was trying to sit up, for the first time. The left upper limb was in its pre-operative state but power in the lower limbs was symmetrical, and the plantar responses were flexor. Tone and tendon reflexes in the limbs were symmetrical. He was beginning to learn a nursery rhyme, but little account can be taken of that advance because he was three and a half months older when he left hospital.

It was thought possible that replacement of the bone flap would not be required because of the likelihood of regeneration of bone, especially after an indolent infection in the field of operation.

The future history of this case is of

importance. The anomaly was extensive and the future could reasonably be considered dubious for the child without lobectomy. He was already retarded before operation.

The boy is now two years old (September 1957) and his fits have not been fully controlled. He spent a week in hospital seven months ago because of an outburst of convulsions in spite of continuing treatment with phenobarbitone gr. ss., b.d.; an increase thereof has been advised. He has periodical brief phases which seem very like "absences".

He has been moving his left hand more and more in the past nine months, but ignores the hand or deliberately avoids using it much in play. He cannot stand or walk unsupported and the earlier promise of language development has not been maintained because his vocabulary is no greater than a year earlier and he became aphasic again with the epileptic outburst.

He is very active, mainly crawling about without evidence of hemiparesis and he can progress erect independently if helped by holding on to furniture. The plantar responses are flexor.

The parents state now that there is left handedness in the family; a maternal uncle, and paternal grandfather of the child are left handed, and his mother has a degree of left handedness, so that there is support for the belief that the

hemisphere affected in the angiomatosis is dominant in this child.

The median "step" of bone at the forehead is still evident and palpable.

CASE VI

YATES, Lucianne: aged 8 years.

Youngest of four children, the others being normal in every way. Born at term, normal except for a facial naevus on the left side.

Her early development was normal, and indeed was considered to be in advance of that of the other children in infancy. She had a three-word vocabulary at the age of 10½ months, when she had her first (nocturnal) convulsion, which continued for about half an hour, either continuously or consisting of a succession of attacks. She was admitted to a small local hospital and further attacks may have occurred. During the first week she developed a gross right hemiplegia and became aphasic.

Her development seems to have had a bad set-back because it was not until she was 4 years old that she was able to try progression with the aid of a wheel-frame, and at that time also she began to learn again to speak.

There were frequent minor attacks in groups at intervals up to the age of 1½ years, in which she stared, made sucking gurgling noises, slight movements of the limbs occurred, and urine was voided. She was receiving phenobarbitone gr.ss. b.d.

After the age of 1½ years the attacks

conspicuously lessened, on the same dose of phenobarbitone, and since then they have taken the form of an "absence" shortly preceding a fall to the ground and voiding of urine.

She became able to walk independently at the age of 5 years. Her right hand has never developed ability for skilled movements. The right facial weakness is slowly diminishing. She cannot be left to run about unobserved because she falls frequently and bruises herself.

She is unable to read any letters and cannot write. Her drawing is very poor. Conversation is good, with some long words. Intellectually she is improving.

Her temperament is satisfactory; she is obedient and helpful, and not malicious. She is clean in her habits.

The skin lesion was treated with Thorium X in earlier years which seems to have been of definite benefit.

Examination showed a well-developed child of friendly disposition and of some intelligence, though co-operation was impaired by distractibility and by limitation of her understanding of simple requirements.

Fig.17

The naevus involved the left cheek as far down as the corner of the mouth, the left side of the nose, transgressing the midline considerably but bounded by the midline at the upper lip. The naevus extended to the upper eyelid and included the skin above the eyebrow, with a broad tongue running up towards the hair-margin. Several linear oval naevoid areas were to be found on the scalp extending to just behind the vertex.

The left half of the upper lip was slightly enlarged. The buccal mucosa was of a reddish purple colour, and this extended on to the upper

alveolus on the left side as far as the midline. The affected alveolus was slightly enlarged, and interdental spaces were increased. The upper teeth were somewhat irregular on both sides, and widely-spaced. Palate normal.

The face was symmetrically developed. The limbs were of equal length and girth.

She was thought to be right handed but had to use her left hand dominantly for skills and for play.

The optic discs were pale with sharp margins: cups symmetrical. Normal ocular tension (by palpation only) and globes symmetrical. The iris on the side of the naevus was browner than its fellow, and that can be seen in Fig.17. Complete right homonymous hemianopia, perhaps with slight central sparing. Right supranuclear facial paresis evident only on smiling.

Grip and elbow movements on the right were about 70% of those on the left: equal power in lower limbs. Poor associated swing of right upper limb. Gait showed a "cast" to the right when bearing weight on the right hip, and in running and hopping the slight motor deficiency of the right lower limb was apparent. However, tendon and plantar reflexes were normal.

On the sensory side all that could be found was a deficiency of joint sense in the fingers of the right hand. Stereognosis was preserved in the

hands.

She was able to obey simple commands. Other aspects of her language ability have been mentioned above. In addition a slurred quality of diction was noted and normal intonation was lacking. Vocabulary and sentence construction was considered to be that of a six year old child.

Electro-encephalography: 7.6.56. (Burden Institute).

This will be detailed later, but it is sufficient now to state that "quietening" of the normal rhythms and responses was seen in the occipital lobe on the side of the naevus, while epileptic discharges were seen from the left temporal lobes and the whole of the right hemisphere.

The radiological evidence in this case is of particular interest. Films made at the age of 2 and 4 years, when the patient lived in the Exeter area, were available by courtesy of Dr.N.S.Alcock. These, with the films of 1956, form a series demonstrating the progressive deposition of cortical calcification. The films are reproduced later, in discussion on the process of calcification.

This patient has been latterly under the care of Dr.St.J.Elkington of London, and she was examined in Bristol with his concurrence, for which due acknowledgment is made.

CASE VII

DAVIES, Megan: aged 24 years.

This patient was seen only because of the clinical interest of the case; advice was not sought because of symptoms referable to the vascular anomaly.

There was nothing of note in the family history. One healthy much younger sister. Full time normal birth, but the infant was slow in starting respiration.

Born with extensive naevi flammei, mainly on the right side of the body.

Seizures commenced at the age of 2 months, in which the eyes deviated to the right, and the limbs on the left side were extended tonically: no convulsions, no pallor: duration about 15 seconds, then sudden recovery. For day after day following the onset she had up to 16 attacks daily, and a gross left hemiplegia was quickly established. Prior to this there had been no asymmetry of limb movements. Anticonvulsant tablets, of uncertain nature and dose, were ineffective, but after a month the frequency of attacks diminished.

In childhood she had long remissions of several months even without treatment, then the attacks would gradually return, larval at first. Those epileptic phases were of several months duration each time, and after some two or three

months with the attacks at their maximum, would again subside progressively.

For some years, certainly after the age of 16 years, the left side of her face has shared in the tonic contraction, but there has been no clonic display in the limbs or face. In many of the attacks she retains consciousness.

She was not incontinent in the attacks during early years but very occasionally urine has been voided about once a year, always in one of many nocturnal attacks.

She remains physically much handicapped and has, for instance, to mount stairs backwards, which she can achieve unassisted. She has to be assisted with her clothes. She is, however, thought at home to show in many respects a normal intelligence. She is good at drawing, and is presently occupied doing one-finger typing of letters for the Spastic Centre in Bristol which she attends daily. She is sweet-tempered but has twice shown violence to her mother, independently of overt epileptic attacks.

On examination she was petite and thin. The naevus covered the whole of the right side of the face except for a white strip which, curiously, corresponds to the fissure between the maxillary and mandibular portions of the face. The naevus was of a dusky purple colour and did not blanch completely on pressure, like the naevi in the preceding cases. Fig.18 shows the extent of the naevus and the transgression of the midline. It

was bounded by the vermilion margin of the lip and the mucosa of the mouth was unaffected.

Fig.18

Naevoid skin was to be found also extending a short distance into the hair-bearing scalp, on the front of the neck, clavicular and upper sternal regions, mainly on the right side; and back, buttocks and lower limbs bore naevoid patches of varied but considerable size. The upper limbs were devoid of birth marks.

There was heterochromia iridis, the right being brown and the left grey-green. No buphthalmos or glaucoma. The sclerotic of the right eye was of a darker tint than normal inferiorly.

Gross thoraco-lumbar scoliosis, concave to the right, with slight kyphosis. The right upper limb was the shorter by about 2 cm.; it was thinner and more delicate in build and the hand was smaller and slenderer. Lower limbs symmetrical except for a smaller left calf (girth 24 cm. as against 25.5 cm.).

Visual acuity normal on both sides (corrected). Complete left homonymous hemianopia. Right ocular fundus not seen because of a "pin-point" fixed pupil. It was not known when this state of the pupil appeared. The left optic disc was pale with normal margins. The left pupil was medially displaced and not quite circular; its reactions were normal. The left eye deviated outwards at rest.

A mild cutaneous sensory depression was found on the left side of the face. No facial paresis. Nothing of note concerning lower cranial nerves.

Gross paresis - almost a paralysis - of the left hand so that she was just able to pick up a pencil clumsily, but power at elbow and shoulder was about half that of the right side. Very poor pronation and supination (left). Loss of power in the left lower limb was slight but the foot was held in the plantar flexed position. Muscle tone and tendon reflexes were subnormal on the left but the plantar reflex was extensor on that side. Abdominal reflexes equal.

Co-ordination of movements in all four limbs was conspicuously poor, especially on the left side. She stood on a broad base and swayed dangerously to either side on trying to walk unassisted.

No depression of touch sensation was demonstrable except on the left side of the face and part of scalp. Pain and temperature modalities seemed to be increased on the left side below the umbilicus, but normal elsewhere up to the face. Joint sense was defective distally in the left upper and lower limbs, and vibration sense was also impaired similarly.

The roentgenograms in this case also are of particular interest for several reasons. The gyriform calcifications extend forward into the right frontal lobe. Further the calcifications nearly reach the calvarium only posteriorly in lateral views and then a broad column of somewhat gyriform shadows, without the double-contouring appearance, extends forwards. In stereoscopic views this anterior extension is plainly seen to be well within the substance of the hemisphere, and it is not quite clear where the cavity of the lateral ventricle lies within this opaque zone. As in all the reported cases, the calcifications fade out anteriorly. This columnar forward extension of calcium deposits has been apparent

in several of the similar reported cases which will later be discussed.

In antero-posterior view the images are too confused to afford further information. The manner in which the median occipital calcifications fall short of the midline is remarkable and rather difficult to explain, as in the other personal cases, unless it be assumed that during development the falx has been bodily shifted to the abnormal side or, more correctly, has developed "off-centre". This is quite probable because there is in this, as in so many other cases, a degree of hypotrophy of the cranial chamber on the abnormal side.

Carotid arteriography (18.7.56) with stereoscopic lateral exposures gave further information in this case. Cortical arteries were seen to extend out normally to the calvarium, thus disposing of the unlikely possibility that the cerebrum was very grossly atrophic. The attached prints (Fig.20a) are stereoscopic.

The arteries posteriorly did not fill so that there was no helpful evidence from the arteriograms as to the state of affairs at the parieto-occipital region, for instance, where it would be most informative in this case.

Burr holes made in the skull would have settled the question but there was no clinical justification for proposing an operation in this

Fig. 19.

Fig.20

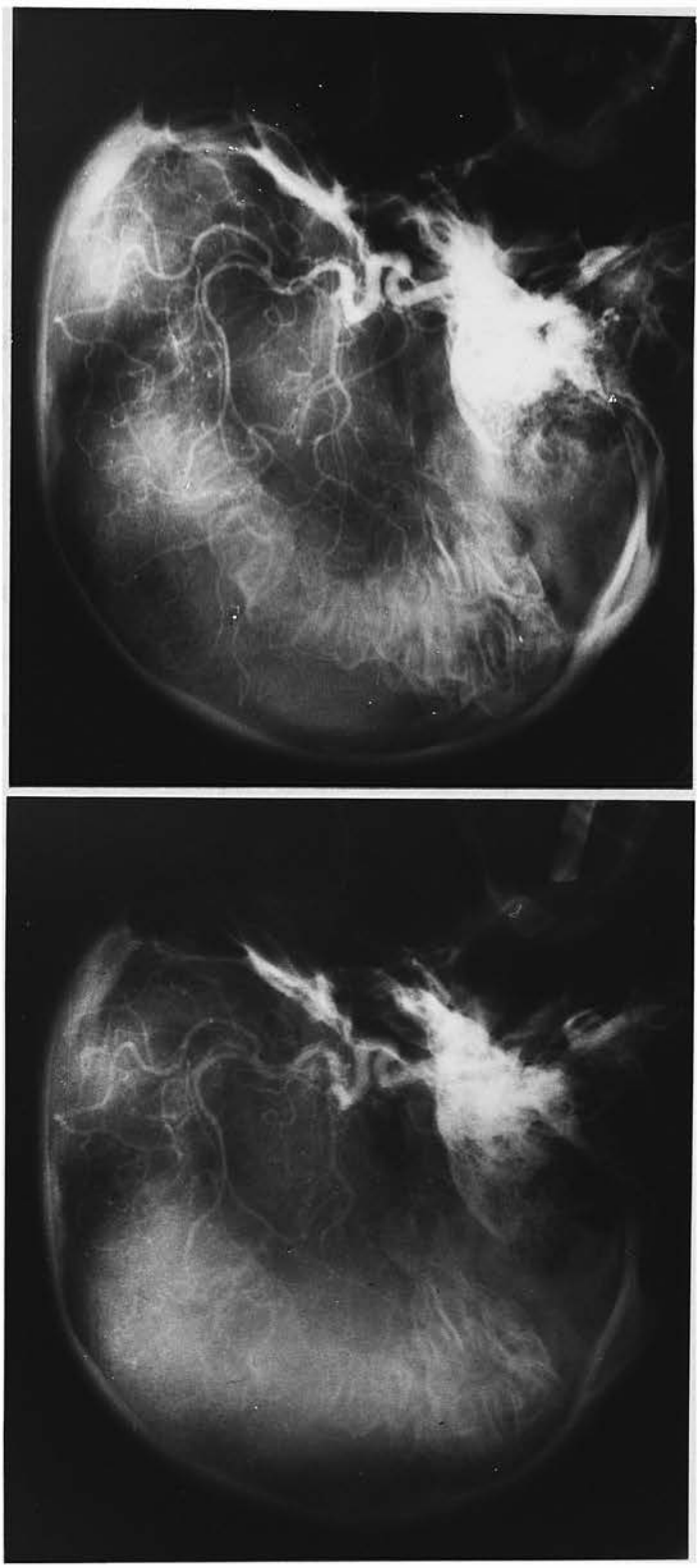


Fig. 20a.

case, particularly as the patient did not seek neurosurgical advice.

Her outstanding physical disability, apart from the palsy of the left hand, was an ataxia.

Taking into account also the lack of hypertonus and weak tendon reflexes in the limbs, there can be little doubt that this patient also has a cerebellar hypotrophy, probably on both sides. Unilateral cerebellar atrophy has been described in a few cases of the Sturge Weber syndrome and will be referred to again in the section Comments on the Literature. Cushing (1906) found a small trigeminal ganglion on the side of the naevus in one of his cases. If a similar abnormality be present in this patient it is of course contralateral to the naevus.

EMBRYOLOGICAL CONSIDERATIONS

It will be noted that in all of the personal cases here described, the facial naevus involves the skin of the forehead and upper eyelid. A survey of the literature confirms that this seems to be almost an unbroken rule in the Sturge Weber syndrome. Only one case has been found displaying the cortical calcifications in the posterior part of the hemisphere which did not conform to this rule.

In contrast, when the naevus lies exclusively below the level of the eye the Sturge Weber changes are not found. Fig.21 illustrates a case studied (by courtesy of Mr.D.Bodenham, plastic surgeon in Bristol): this patient has had no hint of epilepsy, there are no intracranial calcifications and he is neurologically normal.

Fig. 21.

A personal case, Fig.22, with a facial naevus has neither intracranial calcification nor epilepsy; the boy, aged 6 years, is mentally retarded.

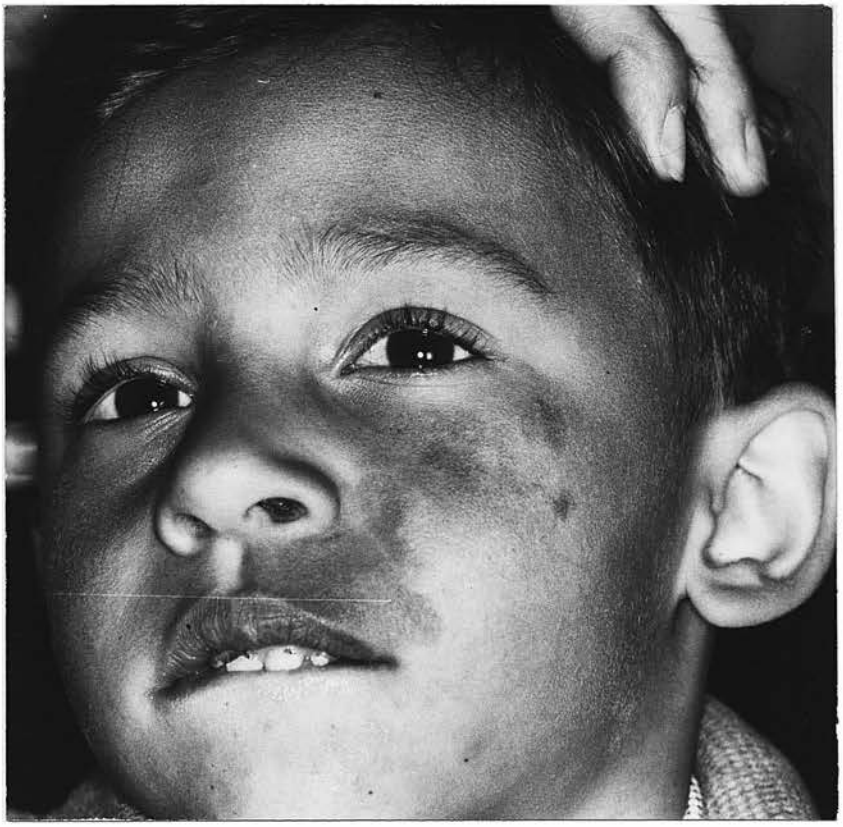


Fig.22

A further Bristol case (under the care of a neurosurgical colleague, Mr.D.G.Phillips) shows sparing of the pertinent area. There are no calcifications but there is a history of epilepsy and a degree of cerebral atrophy has been revealed by air encephalography. No direct information is to hand about the vasculature of the brain in this case.

Fig.23

Figs.24 and 25, from a paper by Ströbel (1942) whose patients were considered to be examples of the Sturge Weber condition, are relevant to this discussion. Neither patient suffered from epileptic attacks, and there were no intracranial calcifications; their neurological syndromes were indefinite but were presumed to be significant. (Reference will be made later to Fig.25 in connection with the distribution of the naevus on the upper lip, which is of some importance).

Fig.24

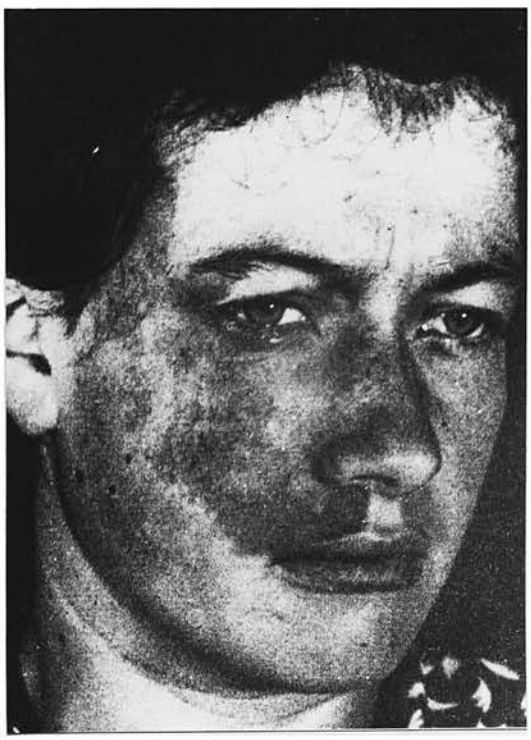


Fig.25

The surveyed literature provides 343 cases with a naevus flammeus of the face, of which 170 cases are typical of the true Sturge-Weber anomaly; in 169 of these the supra-ocular part of the face is involved. On the other hand there are very many cases described as examples of the Sturge-Weber condition (in children or adults) in which the characteristic gyriform calcifications are lacking as evidence of intracranial angiomatosis, and in many there is no history of disturbance relating to the central nervous system. In all of those the supra-ocular part of the face is largely or completely devoid of naevoid skin.

All these facts seem to establish some significance in the presence of the naevus in the supra-ocular part of the face. This point was discussed by Kautzky (1949) who endeavoured to trace a common nerve-supply for the supraorbital skin and the meninges posteriorly, and postulated a parasympathetic overactivity in the embryo as the cause of the cutaneous and meningeal vascular anomalies.

Yakovliev and Guthrie (1931) see an influence of the sympathetic nervous system suggested in the morbid anatomy of the condition in some cases.

The curiously wide separation of the two main manifestations of the disease has long occasioned

comment. It is pertinent that the juxta-ocular portion of the face, and the visual part of the cerebral cortex are concerned in the malady. The work of Streeter (1918) on the early development of the vascular system of the head in human embryos provides some clues.

A preliminary generalisation of Streeter is worth quoting, though it is not relevant to the present argument:

"The embryonic vascular apparatus is continuously adequate and complete for the structures which it serves at any particular stage. There are no apparent ulterior preparations at any time for the supply and drainage of other structures which have not yet made their appearance. For each stage it is an efficient and complete going-mechanism, apparently uninfluenced by the nature of its subsequent morphology".

There would seem to be no "stages" in embryonic development, which is in reality a continuum. Stages are however a descriptive convenience and necessity.

According to Streeter the neural circulation apparatus consists first of primordial endothelial blood-containing channels which are neither arteries nor veins; they are the fore-runners of the differentiated blood vessels. Over the

forebrain and midbrain the primitive vessels have a plexiform arrangement; this is peculiar to the fore- and midbrain.

For convenience Streeter defines five periods up to the formation of arteries and veins of the head recognisable in their adult form. In the first period the plexiform arrangement noted above is present. In the second, primitive arteries, capillaries and veins are differentiated; for the first time they become architecturally suited to the flow of circulating blood. The third period sees a lamination of the primitive head circulation into three layers - for the brain wall, for the dura and membranous skull, and for the skin. The layering process begins at the base of the skull and extends towards the vault and vertex. In this manner the cerebral vessels are progressively separated from the dural vessels. Similarly the superficial vessels of the head become isolated by the laying down of the primordium of the membranous skull. After this the course of development of the superficial vessels is quite independent of that of the dural and cerebral systems.

The fourth and fifth periods are concerned with adaptation of the circulation to the rapid growth of the brain and particularly of the hemispheres, and the maturing of the vascular pattern to a recognisably adult form.

It is of interest that Streeter found the vascular pattern to be virtually constant in different human embryos of comparable size.

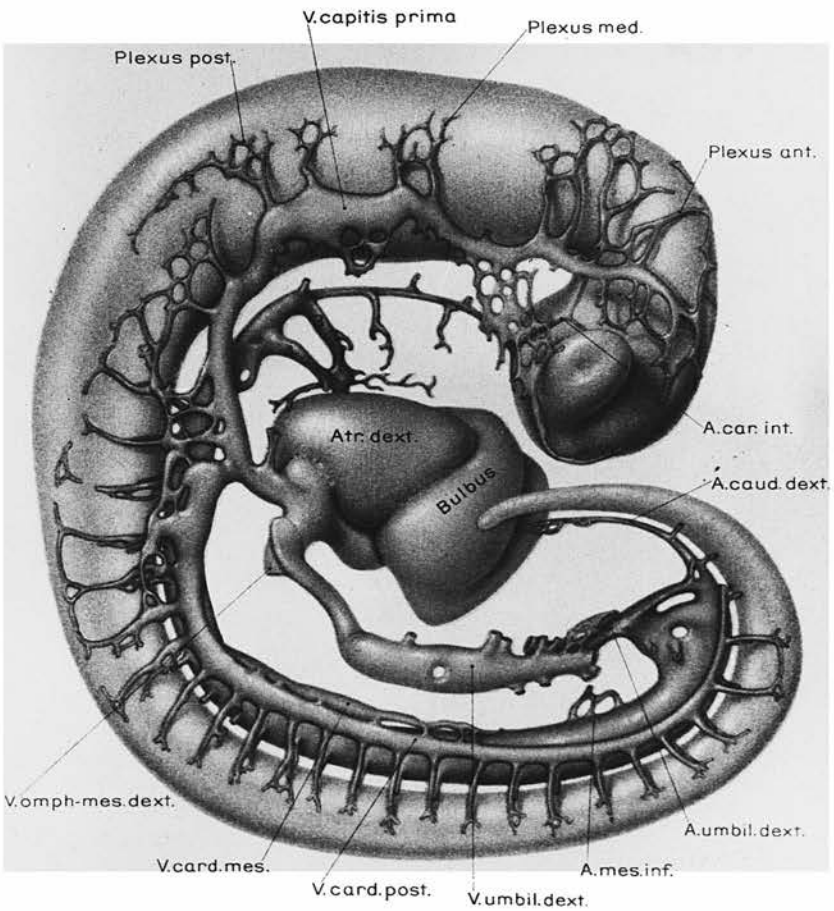


Fig. 22

Fig.26

Above is a photograph of Streeter's reconstruction (Fig.26) of a 4 mm.(crown-rump) embryo.

The cerebral hemispheres are represented only by that small part facing the bulbus of the primitive heart. The close relationship of the optic vesicle to the whole of the hemisphere is obvious, and it would seem permissible to infer a

closer juxtaposition of the tissues which are to form the visual apparatus, earlier still in development.

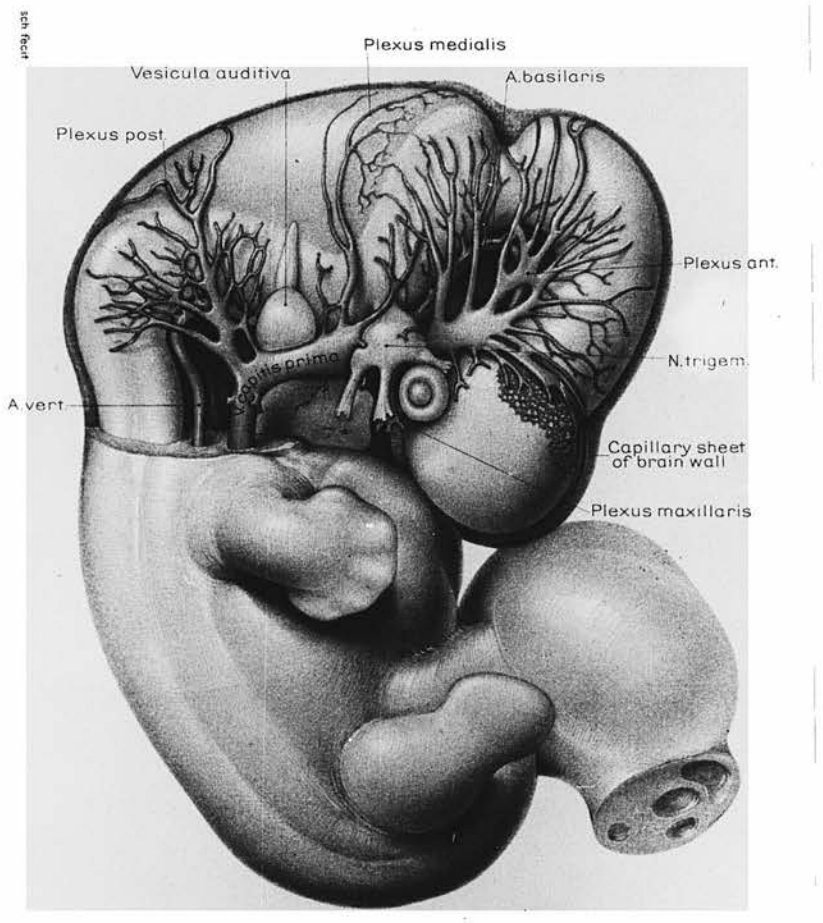


Fig. 24

Fig.27

The state of the circulatory apparatus in the 11.5 mm. embryo is illustrated in Fig.27. The plexiform vessels on the surface of the primitive cerebrum are figured only in the occipital region for clarity, but are to be regarded as investing the whole of the cerebrum and midbrain. The primitive eye has moved away from the occipital

region of the hemisphere. At this stage the cleavage of blood vessels into their three layers is not complete, but the independence of the cerebral blood vessels has been well established.

The theory can be advanced that the Sturge Weber type of vascular anomaly appears exceedingly early in development, at a time when the ectoderm which is to form the skin of the upper part of the face overlies that part of the neural tube destined to form the occipital lobe. The superficial and deep manifestations of the vascular maldevelopment become widely separated with growth of the cerebral hemisphere.

A further theoretical point emerges. If the supraocular area of ectoderm at first overlies the primitive occipital lobe then the ectoderm for the lower parts of the future face might well be related contemporarily to the primitive mesencephalon and mid brain. Streeter has indicated the limited extent of the primordial vascular plexus in his first stage, which may explain the absence of the Sturge-Weber type of angiomatosis from the midbrain, and cerebellum particularly, even when the naevus affects the whole of one side of the face.

It is further to be noted that the venules in the angiomatose area of the brain are almost entirely of small and uniform calibre, with a plexiform pattern suggestive of derivation from an

embryonic vascular network, probably having no directional flow of blood within it at an early stage.

It is now of interest to speculate what might be expected if an angiomatous malformation affecting the skin of the face and the brain were to appear later in embryonic development, when the proportions of the cerebral hemispheres had been more defined and the developing blood vessels were more mature. It would be reasonable to suppose that the cerebral lesion would be located more anteriorly in the cerebrum. A further permissible fantasy would allow that the vessels in the lesions might be of larger size, having developed abnormally at a later stage in embryonic life. There is no shortage of cases conforming to this idea.

By courtesy of Dr.R.M.Norman (Regional Neuropathology Laboratory, Bristol), his photographs of one of his cases are here reproduced.

Fig.28

The patient, aged 36, was an inmate of an epileptic colony. A clinical description was given by Bates (1937) under the title of "naevoid amentia". Long-standing motor defects were evident in the contralateral upper limb and the optic cup was deep on the side of the naevus. Radiological examination showed gyriform calcifications in the Sylvian region on the side of the naevus.

In due course the specimen became available. Enlarged veins were evident at the surface of the brain on both sides and on the right side (that of the naevus) a limited area of angiomatosis of Sturge Weber type overlay cortex in the Sylvian region: the calcifications corresponded to this area.

On coronal section of the hardened brain at

posterior frontal levels an intracerebral angioma was revealed on the left side. (Fig.29): no photograph is available of the section of the right hemisphere, which however showed little penetration of its substance by abnormal veins, in contrast to the state on the left side.

Fig.29

Cortical calcification was present only on the side of the facial naevus. The radiological appearance of the specimen is shown in Fig.30.

Fig.30

This is an important case, in showing that the Sturge Weber anomaly can occur coincidentally with intracerebral angioma, but it is a rare accompaniment. Lichenstein (1954, Case 3) and Livingston et al. (1956, Case 5) describe cortical calcification in patients with facial naevi and intracerebral angioma, and Giampalmo (1940) - without a naevus.

The facial naevus in this case of Bates and Norman was rather verrucose, a feature notable in some other cases of intracerebral angioma with facial naevus. It is tempting to speculate that

this quality of the naevus might corroborate the hypothesis of a rather later embryonic origin of the vascular anomaly in cases of this type, which in any event ought to be excluded from the Sturge Weber category. The angiomata it is to be noted were not occipital or parietal in this case, which might be permissible as an argument supporting the later origin of the vascular anomaly in this and similar cases. The lesion in Kalischer's case was Sylvian in location; his figures indicate the angiomatous trend of the vessels which did not, however, penetrate into the cortical substance and in that respect conform to the morbid anatomy in the Sturge-Weber anomaly. The absence of pericapillary calcification in his sections is odd, and although his case has been here included in the "acceptable" group, Kalischer's case (aged 1½ years) may not have been truly an example of the Sturge Weber malady as strictly interpreted.

THE "TRIGEMINAL" DISTRIBUTION OF THE FACIAL NAEVUS.

For long it has been traditional to relate the distribution of the facial naevus to that of branches of the trigeminal nerve, and Cushing (1906) placed emphasis on this aspect of the malady. If we examine the evidence critically, however, objections to this conception appear.

In the first place in nearly every case the naevus transgresses or falls short of the midline

in places, yet the exactly median limit of a trigeminal sensory field is common knowledge.

Fig.31

The second point concerns an important clue which is to be found in Case II. Fig.31 demonstrates that in the upper lip the outer margin of the philtrum forms the boundary of the naevus; in the mouth the naevus comes again to the midline at the upper gums. (Fig.32).

In this child it can be inferred that the ectoderm of the globular process of the maxilla was spared. The boundary here of the naevus conforms to the defect in cases of hare-lip.

Fig.32

This is not a unique case. Two further illustrations from the literature are given.

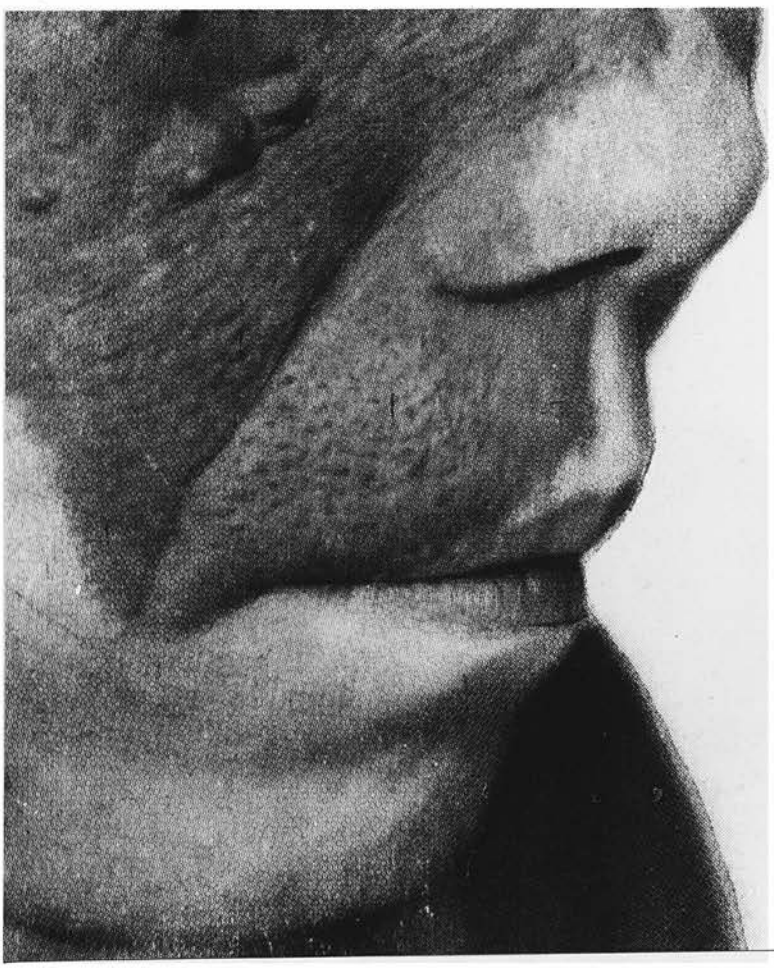


Fig.33

Fig.33 is from a monograph by Larmande (1948) reproduced from a medical museum in Paris, without clinical details.

Fig.25., from the paper by Ströbel (1942) referred to previously, insofar as the naevus is concerned illustrates the detail under discussion.

Thirdly, the area affected by the naevus in a case such as that reported by Kleyntzens (1948) surely suggests the distribution of the naevus is a matter of chance (Fig.34).

Fig.34

There seems to be no salient objection to the assumption that the distribution of the facial naevus is determined by the lay-out of the processes and fissures in the development of the face, and that the trigeminal relationship is secondary and fortuitous. Krabbe (1955) in a Festschrift expresses the same view.

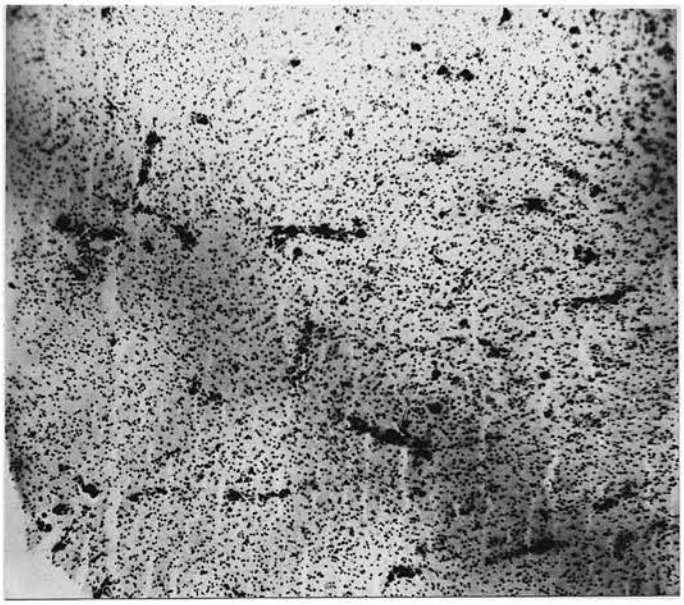
Virchow (1887) considered that the embryonic clefts might be of importance in determining the boundaries of a facial naevus. He went on to propound a theory that "small irritative phenomena" in the vicinity of the clefts might cause proliferation of blood-vessels. This hypothesis is not attractive.

In passing, the dominantly unilateral affection in cases of Sturge Weber disease is noteworthy.

THE INTRACEREBRAL CALCIFICATION.

It is generally agreed that the intracerebral calcifications in the Sturge Weber malady are to be found characteristically on the outer surface of cortical capillaries. In addition, mineral concretions which can attain a relatively large size, lie within the substance of the cortex, and microscopically also within the subcortical white matter. The cortical concretions are responsible for the distinctive gyriform shadows radiologically apparent in typical cases. These shadows are often referred to as "double-contoured", an appearance which is manifestly due to calcification in opposing gyri in a sulcus, in end-on projection, (and not quite as figured diagrammatically by Bergstrand, Olivecrona and Tönnis).

The question arises at what age does the calcification begin, microscopically and macroscopically.



The material obtained at operation in Case V. at the age of one year shows calcification in that instance to have been under way in the capillaries of the cortex (Fig.35). The hardened specimen could be cut without any suggestion of "grittiness". As expected, the X-ray films of the skull were devoid of any visible calcifications.

Obviously a histological study of the cortex of affected infants at birth and subsequently would fill in this gap in our knowledge. The difficulty is that the epilepsy is very seldom neonatal in onset. In the light of a recommendation to be made later in this Thesis, opportunities for

histological investigations early in life should become less rare.

Fig.36

Fig.37

Fig.38

The series of skiagrams of Case VI. is pertinent to this topic. At the age of two years (the first examination) the typical calcifications are just discernible, and they have been increasing in area and opacity in the two later films at ages four and seven years. This child is now eight years of age, and if, as seems probable, she has no operation she will provide information as to the age at which the process of calcification in her case becomes stationary.

In Case III. some consolidation in the radiological appearance of the calcifications occurred between the ages of 14 and 18 years.

Thirty descriptions have been noted in the literature of examples of the Sturge-Weber malady in the very young, confirming the absence of

radiologically visible deposits in infancy. Worster-Drought (1948) had a case in which calcifications were absent at the age of 8 months, and had appeared at the age of 18 months.

It seems fairly certain that the characteristic deposits begin to be discernible radiologically during the second year of life.

A possible relationship between the degree of cyanosis in the vessels of the angiomatose area and the degree of deposition of calcium in the brain falls next for consideration.

The clinical material of this Thesis affords five cases in which it can be said without exception that marked local cyanosis was apparent at operation only in those patients with dense cortical calcification. Tönnis (in the monograph with Bergstrand and Olivecrona) comments on the extreme cyanosis of the abnormal venules in his case at operation. The calcifications in his case were radiologically conspicuous.

In Case III, calcification and cyanosis were slight, and in Case IV. proportionately rather more in evidence. In the infant (Case V.) the meningeal vascular lesion was very definite and the vessels close-packed, but the blood circulating within them was not cyanotic. It is quite probable that in time gross cyanosis and calcification would have appeared in this case. This topic of calcification will be discussed further in the section dealing with histology.

Further light on the potential importance of local hypoxia in the deposition of calcium in the tissues is thrown by Alexander and Woodhall (1943), who described their findings in three cases of acquired focal damage to the cerebral cortex. The lesions were epileptogenous and intracortical calcification had occurred. Although the lesions had been acquired in three different ways the histological feature common to all was the persistence in a patent state of a proportion of the capillaries dispersed fairly evenly throughout the cortex in the abnormal area.

Fig.39

Fig.39 shows the vascular arrangement in normal cortex, and Fig.40 that in their first case.

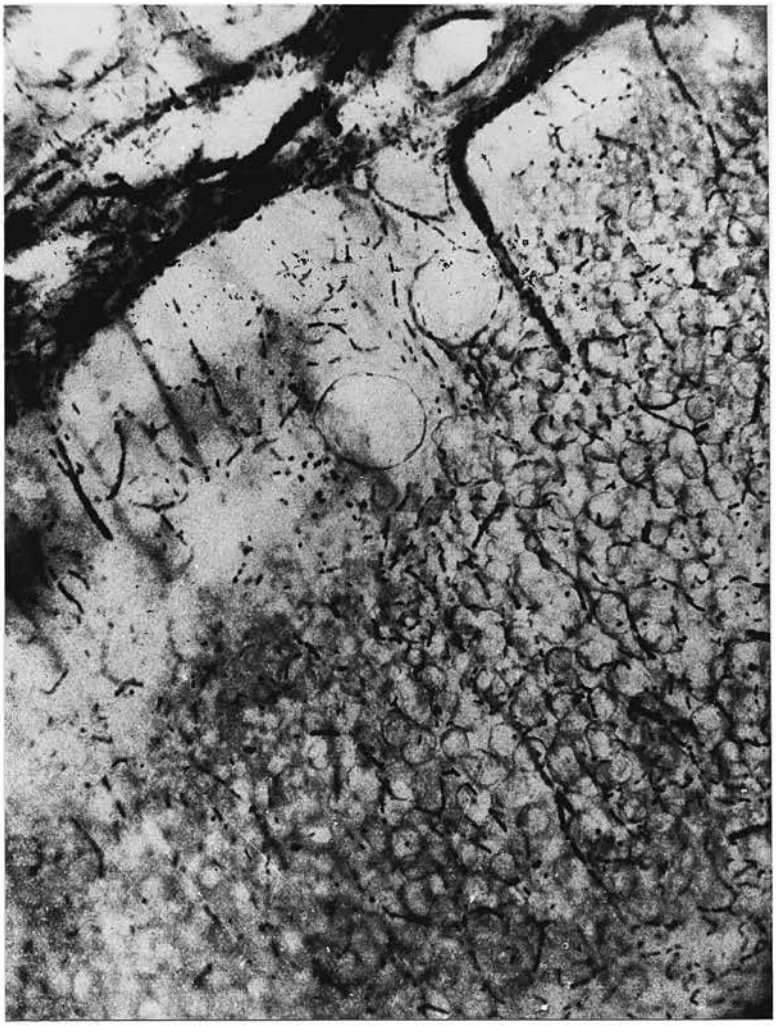


Fig.40

The calcifications were confined to the grey matter of the cortex, with sparing of the outermost and of the sixth layer in the less havily calcified areas. The deposits were interstitial and appeared to have been precipitated at random, without relation to particular structures. There was no calcification on the blood vessels, which the

authors pointed out, contrasted it with the Sturge-Weber condition and with the cortical endarteritis calcificans of Gayelin and Penfield (1929). The adjacent cortex, and the subjacent white matter, were normal

Fig.41

Figs.41 and 42 show the disposition of the calcium deposits in one of their cases.

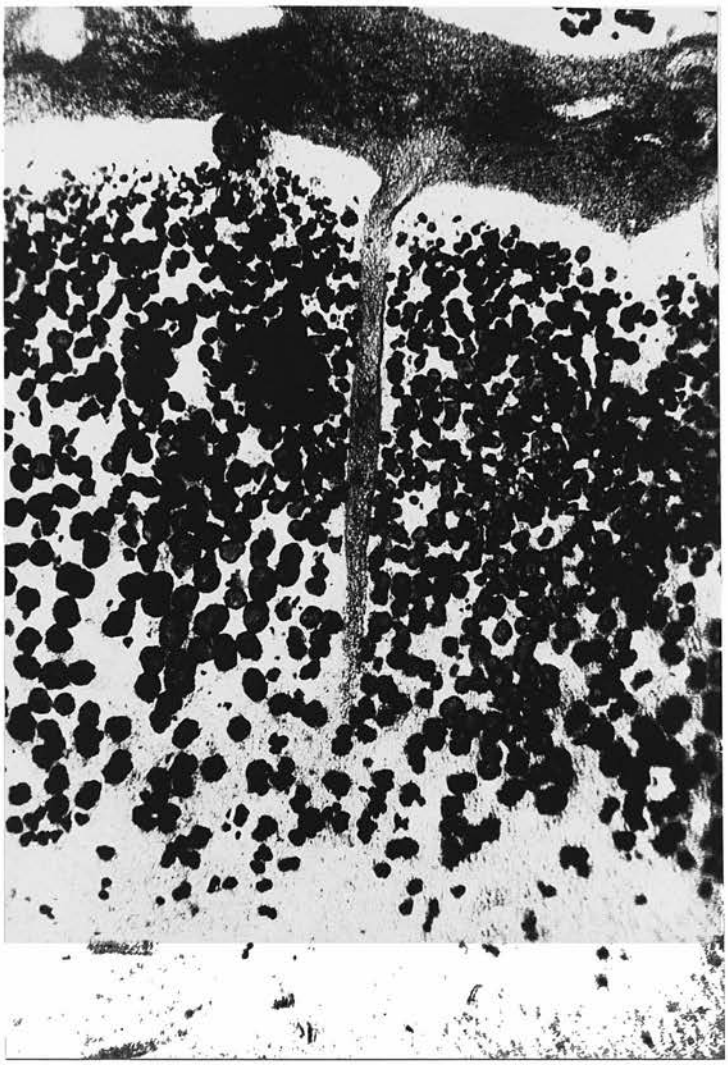


Fig.42

The authors were impressed by the large number of histologically-normal neurones persisting among the calcific deposits, and by the evidence here and there of recent death of a neurone, although the lesions were of many years standing. It seemed as if there was a continuing "fall-out" of neurones with the passage of time. The persistence of functioning neurones in the pathological area was felt to have significance in relation to the epileptogenic nature of the lesion.

All three of the patients were benefited by resection of the diseased area. Meningeal angiomatosis was not seen in any of the cases.

Alexander and Woodhall postulate that the breakdown of lecithin, which liberates phosphoric acid (Baldauf, 1906; Hanes, 1912), and the streaming blood in the remaining capillaries, provides a continuous source of calcium to combine with phosphoric acid. As will be seen later, the concretions consist largely of calcium phosphate.

The authors were unable to explain why the calcification in their cases was exclusively cortical, but suggested that the lipoids of white matter might furnish insufficient amounts of phosphoric acid. They mentioned the application of these ideas to the Sturge-Weber condition, and thought that the venous stasis was the primary state and the calcification secondary. They had no explanation for the perivascular deposition of calcium in the Sturge-Weber anomaly.

Lichtenstein (1936 and 1954) thinks that a progressive deposit of calcium salts on the capillary walls could well cause hypoxia of the tissues. He supposes that the small hyaline core often found at the centre of the larger concretions represents the remains of a blood vessel. This hyaline core was also noted by Volland (1912) who thought therefore that hyaline degeneration in vessel walls was the precursor of the calcification. Lichtenstein's conception of a vicious circle in

regard to permeability of the capillaries is helpful. It is interesting to note also that he has found pericapillary beading with mineral salts identical with that seen in the Sturge Weber anomaly, in a case of lead encephalopathy.

Taking the foregoing points into consideration, a chronic sluggishness of capillary blood flow, probably increasing in degree during childhood in the Sturge-Weber condition, would seem to be the basis for the cortical calcification. The appearances at operation suggest that the network of angiomatose venules, often covering a large area, has an inadequate drainage into larger veins. The evidence from arteriograms, in some cases, of paucity of arterial supply to the pathological area cannot be accepted at face value as indicating a throttling on the arterial side because a deficient outlet of venous blood from a territory must retard arterial filling.

The writers quoted have all stressed tissue-hypoxia as the operative factor but as will be seen later, in discussion on the electro-corticogram findings in the personal cases, the interference with gaseous exchange across the capillary walls may have as its more pertinent effect an increase in carbon-dioxide tension in the tissues served by the calcifying capillaries. But when hypoxia is due to impairment of the speed of circulation in living tissues, oxygen deficiency

and carbon dioxide excess are directly related and it may be impossible to separate them in theoretical deduction relevant to the issue.

Chemical Analysis.

In the literature a difference of opinion exists as to the mineral constituents of the abnormal cortex in the Sturge Weber anomaly, the point at issue being the content of iron.

Eaves (1926) reported a 500-fold increase in calcium and a 200-fold increase in iron in one case. Peters and Tebelis (1937) found no iron (but give neither technical details nor figures). Wachsmuth and Lowenthal (1950) criticised the analytical methods of Eaves, and found no increase of iron. Lichtenstein and Rosenberg (1936) championed the ferruginous nature of the deposits, but relied on histochemical methods alone, whereby they seemed to prove there was no calcium in the deposits.

By good fortune it happens that A.H.Tingey, who investigated the iron and calcium content in normal brain (1937), is now working with Dr.Norman in Bristol. Tissue from four of the personal cases was submitted to him for analysis, with special reference to the findings of Eaves. An

extract of his results follows, (Tingey, 1956).

Formol-fixed cortex.	Inorganic Iron (mg./100g.of wet brain)	Total Calcium (x normal = 13.6mg/100g.)
Normal	3.24	
Case I	2.27	x 723
Case II	1.18	x 122
Case III	3.37	x 36
Case V.		x 7.7

Obviously the figure for calcium will depend on the size and number of concretions in the tissue sampled.

Tingey criticises the analytical method of Eaves and comments that iron was not estimated as such but by weighing a residue after extraction with hot strong acetic acid, whereby a fallacy could arise.

The cortical concretions always give the Prussian-blue reaction for iron, and Tingey suggests that adsorption of iron, readily available in cerebral tissue, onto the concretions, is the probable explanation for the colour reaction.

The calcium was found by Tingey to be present mainly as phosphate and carbonate. This might be inferred as significant in view of the Barnes and Woodhall theory involving free phosphoric acid,

and the possibility of a high parenchymal CO_2 tension.

RADIOLOGICAL NOTE

It is very common indeed for the appearance presented by the gyriform calcifications to present seemingly conclusive evidence of gross shrinkage of the brain in some areas at least of the lesion. Yet personal experience and the accounts of operations in the literature exclude the presence of the subdural fluid which would necessarily have to occupy the dead space; this space often has the appearance of being one or two centimetres in depth - far greater than the subarachnoid space could accommodate.

The possibility that this appearance might fallaciously result from the divergence of X-rays from the anode was considered, (Fig.43). Dr.K.H. Gaskell (Frenchay Hospital) produced lateral films of the skull of the patient (Case VII.) with short and long target-distances and comparison showed that the relationship of the calcific shadows to that of the cranial profile was not significantly altered. Even right and left lateral projections under these conditions showed no significant change in the relationship.

In truly-positioned antero-posterior views of the skull, the medial occipital calcifications usually fail to reach the midline and there is no argument about the existence of some degree of cerebral atrophy in most cases.

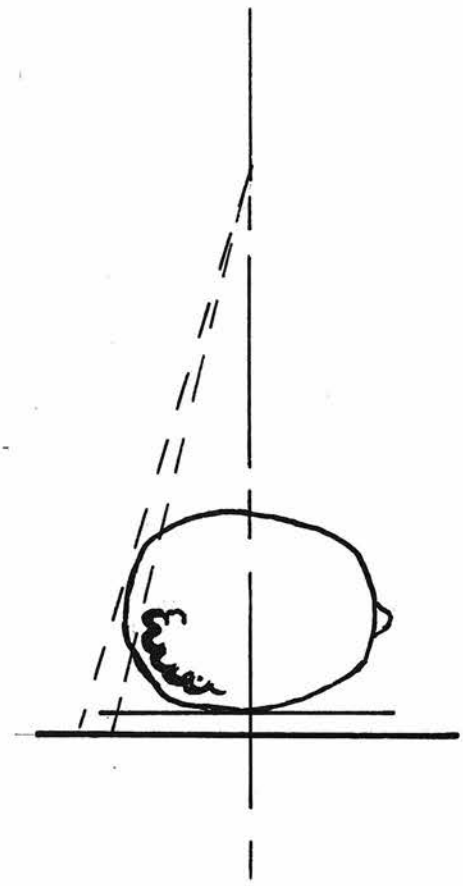


Fig. 43.

The stereoscopic films of the first two personal cases show that the appearance of shrinkage seems greater when the films are inspected singly, but even so in Case I., with three-dimensional viewing, the calcified gyri seem undoubtedly to recede unduly away from the calvarium in places anteriorly.

Case VII., remarkable on account of the marked recession of the calcifications away from the calvarium as the lesion is traced forward, yielded

stereoscopic arteriograms which showed some cortical arteries where they would be expected at a normal cerebral surface, and at a distance from the calcifications. It is unfortunate that the filling in these arteriograms is rather early to show the vessels posteriorly. More information is wanted about this type of case; no record of an autopsy has been found. The case of Lichtenstein (1954) had frontal and occipital calcifications which were superficial and no information relevant to this Case VII. is forthcoming from his autopsy findings.

Cranial asymmetry is very common, the capacity being reduced on the side of the vascular anomalies. This is exemplified in personal cases I. II. IV. and VII. Cranial hypotrophy seems not necessarily to be related to the extent of visible calcifications. In Case II. they were occipital yet there was asymmetry. Rullan and Rifkinson (1955) on the other hand comment on the symmetry of the cranium in their case notwithstanding calcification of the whole hemisphere.

Larmande (1948) has made much of an enlargement of the facial tissues and skull structure anteriorly, particularly of the frontal air sinus, on the abnormal side, which suggests to him a unilateral acromegaloid state. A few other writers describe enlargement of one frontal air sinus. Dr.Norman found a large frontal air sinus

in his case on the side of the facial naevus; and a curious and apparently unique minor anomaly of development of the frontal bones was noted in personal case V.

Larmande finds evidence of endocrine abnormality in the obesity noted in a minority of cases, and in the occasional sexual hypotrophy. It seems clear, however, that evidence of endocrine disturbance is generally lacking in the recorded cases; moreover retardation of the onset of menstruation has not been noted as a feature of the syndrome.

THE EPILEPSY

The epileptic part of the syndrome merits special consideration. The onset of fits almost invariably brings the patient first to the notice of the clinician; few parents seek advice for cosmetic reasons only during infancy. Further, histories given in the literature, and in this Thesis, indicate that after a bout of convulsions the intellectual development of the patient may receive a serious and abrupt set-back. On the basis of the functional damage which the developing brain appears to suffer when epilepsy supervenes, an argument can be made out for early surgical intervention in the expectation of forestalling the disaster of a status epilepticus in those who exhibit the Sturge-Weber anomaly implicating the supra-ocular region of the face.

In the majority of recorded cases the first convulsions have been observed during the first year of life in those with the more extensive facial naevi and by the age of two years in the lesser examples.

As might be expected the convulsions are very frequently focal in type, manifest on the side of the body contralateral to the naevus, but of course often become generalised in individual attacks or bouts of attacks. Frequently there are histories of long remissions from the epilepsy in the early years, with anticonvulsant treatment and

sometimes spontaneously. Sometimes the pattern of attacks changes in detail after a long remission.

In parallel with what is found in subjects with epileptogenic cerebral lesions of other types acquired early in life, some stunting of growth and development of the contralateral limbs is common. The skull also often exhibits a reduction in cranial capacity on the side of the vascular anomalies.

In the histories of children with the Sturge-Weber anomaly there is a general trend towards increasing difficulty of control of the attacks medicinally, with the child falling farther and farther behind in intellectual capacity.

The histories of Cases IV. and VI. deserve study; they have a message. The aphasic imbecile aged 11 years is said to have acquired a vocabulary of about a dozen words before an epileptic storm at the age of 11 months swept all speech from her. The child of 8 years, at the age of $10\frac{1}{2}$ months well in advance of her siblings at a comparable age, ceased to speak for three years after her fits began, and was at the stage of a child of about five years in speaking and learning when seen.

On the basis of those two histories alone it would seem that a case could be made out for early resection of the angiomatous section of the occipital or parietal lobe, before the epileptic state has been given a chance to work its havoc.

In that connection the after-history of Case V. will be of importance, but even in that case operation may have come rather late, because the infant is already retarded: if he overhauls his handicap as the years pass the operation in that case will have been well-justified, for there is little doubt that otherwise an institutional life would have been a certainty for him later.

This raises the question, what happens to Sturge-Weber patients? Do any of them reach middle-age, for instance, or have they mostly succumbed in status epilepticus or with intercurrent disease at a relatively early age? Only a survey of the population in institutions for the epileptic and feeble-minded could provide the answer. It is difficult to recollect having seen any adults at large in the general population showing the Sturge-Weber type of naevus flammeus, (as distinct from the deep purple warty naevus, which is perhaps associated with the cavernous and racemose types of cerebral angioma).

It would be fallacious to ascribe all of the intellectual retardation to epilepsy in these patients. The evidence of the asymmetry of the skull, of the lesser volume of the affected hemisphere in some post mortem cases, the stunting of growth of contralateral limbs and, as in one of Cushing's cases, atrophy or dysgenesis of the ipsilateral hemisphere of the cerebellum, all

points to structural deficiencies far wide of the very obvious cerebral lesion. It would be rash to believe that all this could be prevented if the epilepsy were forestalled or early terminated. Nevertheless if a number of infants with the Sturge-Weber anomaly, who have had the cerebral lesion resected early in life, were studied and recorded, some inference could be drawn as to the extent to which epilepsy augments the disabilities of these children. The post operative histories in some of the cases presented in this Thesis suggest that the deleterious effect of epilepsy is quite considerable.

ELECTROENCEPHALOGRAPHY

The remarkable pre-operative tracing obtained in Case I. is reproduced in Fig.44.

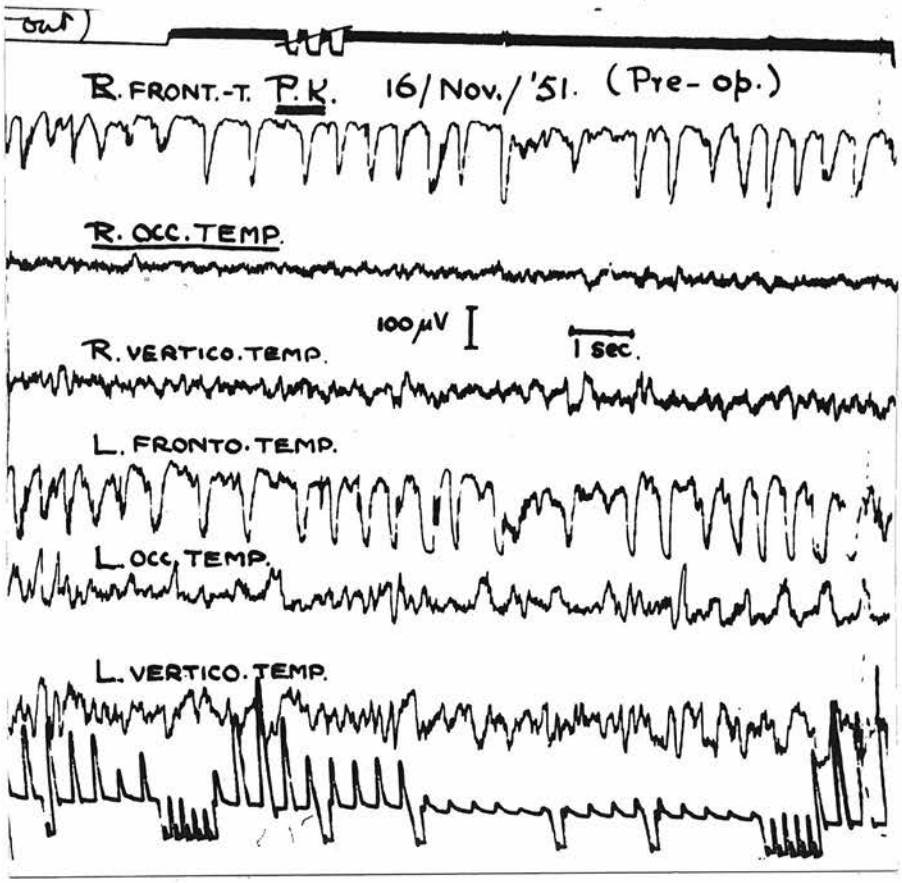


Fig.44

The recording was made by Dr.Grey Walter (of the Burden Neurological Institute) and he commented on the remarkable and unexpected electrical inactivity revealed in two of the gains - those deriving from the scalp overlying the calcified region of the brain.

The recording in Case II., with a much more localised calcification, was much less impressive. On the pathological side there were NO normal

rhythms, only very widespread complex slow activity with occasional brief epileptic complexes involving all areas, sometimes spreading to the right side, when they interrupted the normal alpha rhythm. Flicker stimulus evoked a small following response on the right, but none on the left. Dr.Grey Walter was of the opinion that the absence of normal activity in this second case suggested complete absence of normal functional connections in the left occipito-parietal region.

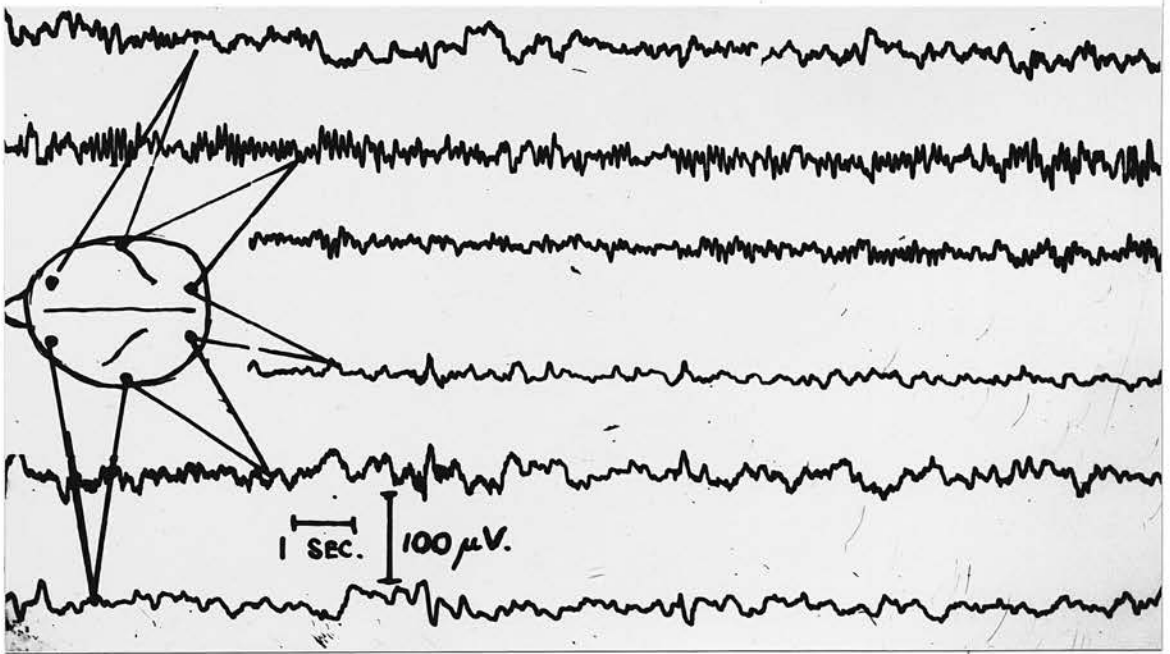


Fig.45

The examination in Case III, with very scanty intracranial calcification, revealed no focal distinctive features. Rhythmic 7-8 c/s. activity was recorded anteriorly on both sides, and in the fronto-parietal regions phase-reversals were obtained. There was no suggestion of a "silent" field.

In Case IV., the idiot girl, recording had to be abandoned because of lack of co-operation.

The records in Case V., the infant, were marred by movement artefact. No strictly localised discharges were apparent. The delta discharges from the occipital lobes were much larger on the side of the naevus (right) than on the left side.

In Case VI. an asymmetry of normal rhythms in the occipital regions was demonstrated, being of subnormal amplitude on the affected left side. Frequent sharp "spikes" and slow waves were focal in the left temporal region. Occasional episodes of high-amplitude delta discharges appeared over the right hemisphere, especially anteriorly. The photic response was small in the left occipital lobe.

Thus, the patient of this series with the most extensive fully developed cortical calcification - and in this patient alone - a region of electrical "silence" was observed.

A comparable observation was made by Green in 1945; he found a localised area of "no activity" in his tracings, situated just behind the anterior margin of the calcified parietal zone in his case. Cohen and Kay (1941) noted a depression "to almost no amplitude" over the affected occipital lobe, and obliteration of the alpha rhythm, on closing the eyes. Delta patterns were evident from other

areas.

The experience of Green, Foster and Berens (1950) and of Lasierra and Aroyo (1955) was similar.

Broager and Hertz (1949) found diffuse spike and wave patterns, with constant phase-reversals in the parasagittal region near the vertex on the side of a typical facial naevus. This patient also showed sinuous occipital shadows radiologically. The authors exposed the premotor region, found a "large naevus", made an en bloc resection of the whole of the premotor area, with benefit to the patient. It is possible that they were dealing with a central angioma. The occipital lobe was not exposed.

Goetze (1953) made observations on five cases of the "Sturge-Weber syndrome" and found reduction of potentials posteriorly on the affected side, except in one case where the potentials were increased and spike and wave patterns occurred. This paper is disappointing. Only one tracing is figured and no clinical details are given of any of the cases.

Vizioli and Floris (1953) described five patients with facial naevi of which only their cases 1 and 2 can be regarded as typical of the Sturge-Weber condition. They describe large voltages of 11 c/s. in one, and 9 c/s. in the other, greater on the non-affected side.

Radermecker (1951) in a series of nine cases had one which was definitely of Sturge-Weber type

and three other probable examples. In the definite case the dysrhythmias of 4 - 6 c/s. were central and bilateral, and in two of the other three cases damping of the tracings and low voltages were recorded from the occipital areas (in one case on the abnormal side only).

The literature, necessarily recent, is scanty and somewhat conflicting in the matter of electro-encephalography, a circumstance which gives added point to the next section.

ELECTROCORTICOGRAPHY

Arrangements were made to record potentials direct from the exposed cortex at the operation in Case I. as an aid perhaps in determining the limits of the required lobectomy. Only a two-channel portable instrument was then available. A representative tracing is reproduced below.

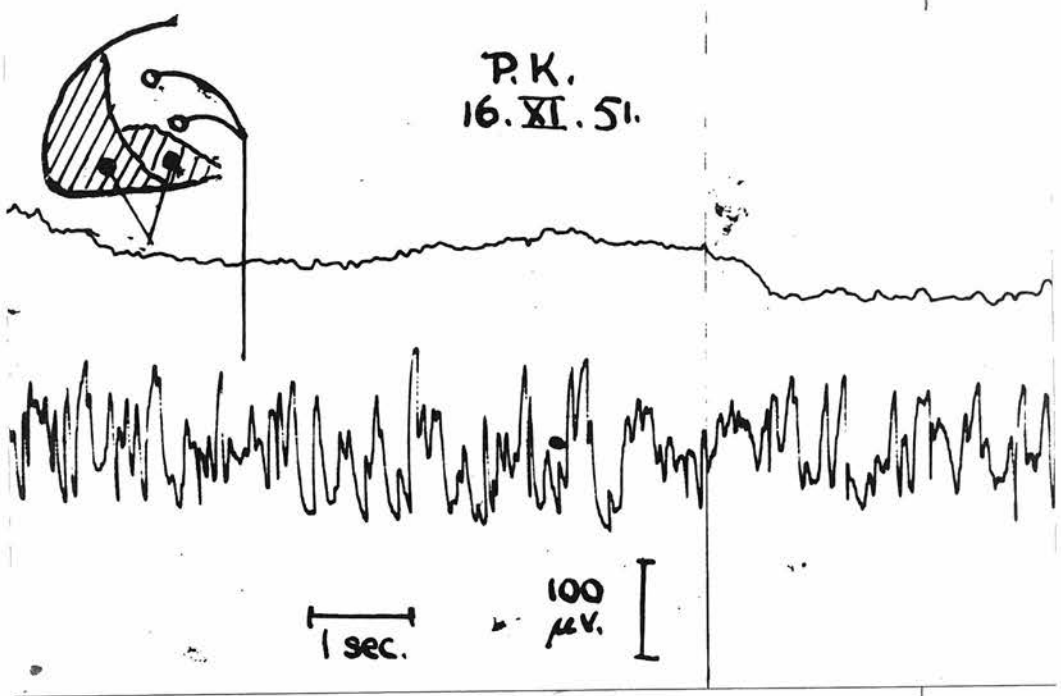


Fig.46

From all of the angiomatose area virtually no potentials were recordable, but in contrast irregular spike activity of high voltage was continuously evident at all areas of the unaffected cortex widely exposed by the craniotomy. It was found that the visible margin of the meningeal vascular anomaly was the boundary of the electrically-inert area. Bipolar derivations oriented parallel

to any margin of the vascular lesion, advanced progressively on to the adjoining cortex, showed that the irregular high voltage activity came into full swing 1 to 1.5 cm. wide of the margin of the angiomatose area. Derivations straddling the margin gave no further information of value.

A depth electrode was available and the inert state of the subcortical structures was demonstrated, extending throughout the rather tough occipital lobe in various directions as far as its medial surface, and obliquely forward until a level close to the corona radiata was reached, approximately deep to the central sulcus. The needle-electrode palpably emerged from gliosed cerebral substance at these depths anteriorly. A representative tracing from gains 5 and 6 cm. deep, obliquely forward from insertion at the parieto occipital convexity is shown in Fig.47.

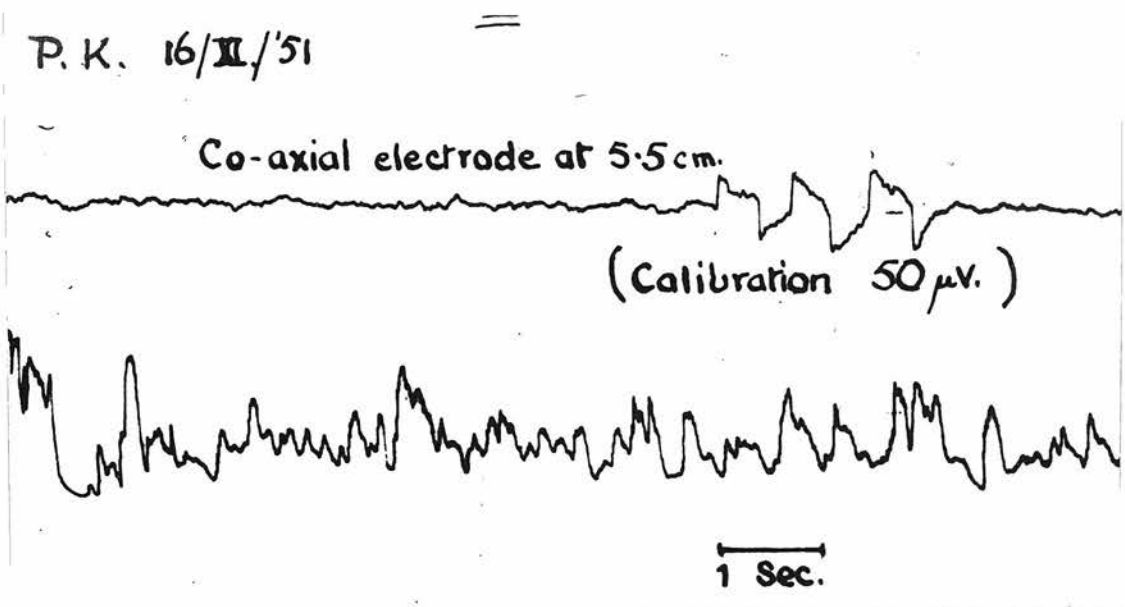


Fig.47

It will be recalled that in Case II. electroencephalography yielded no focus of relative electrical inactivity, yet the electrocorticograms were similar to those of Case I. (Fig.48). Depth recordings were not made.

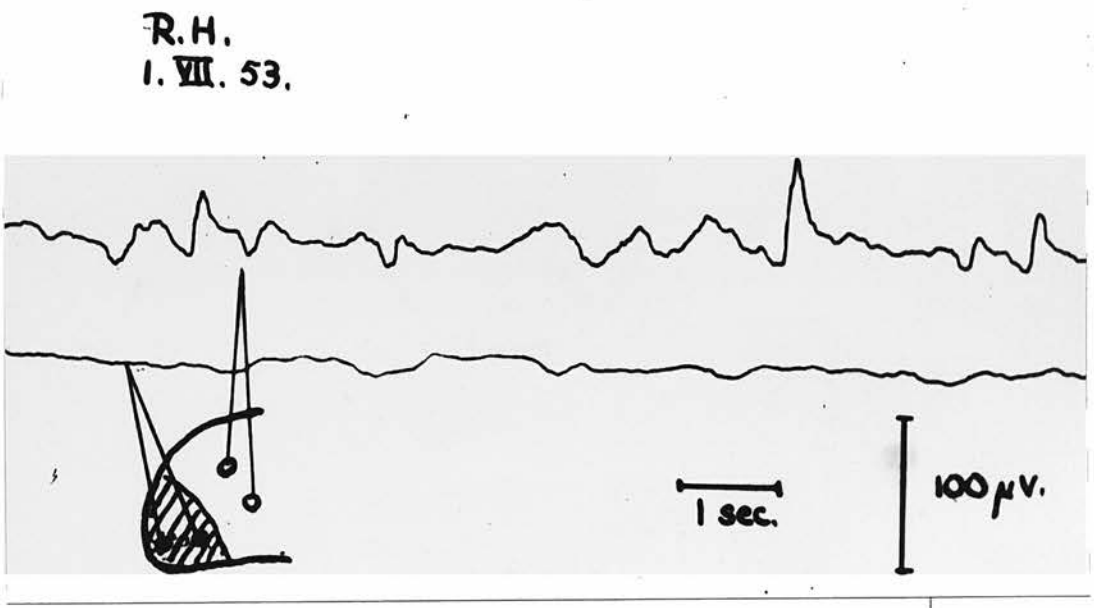


Fig.48

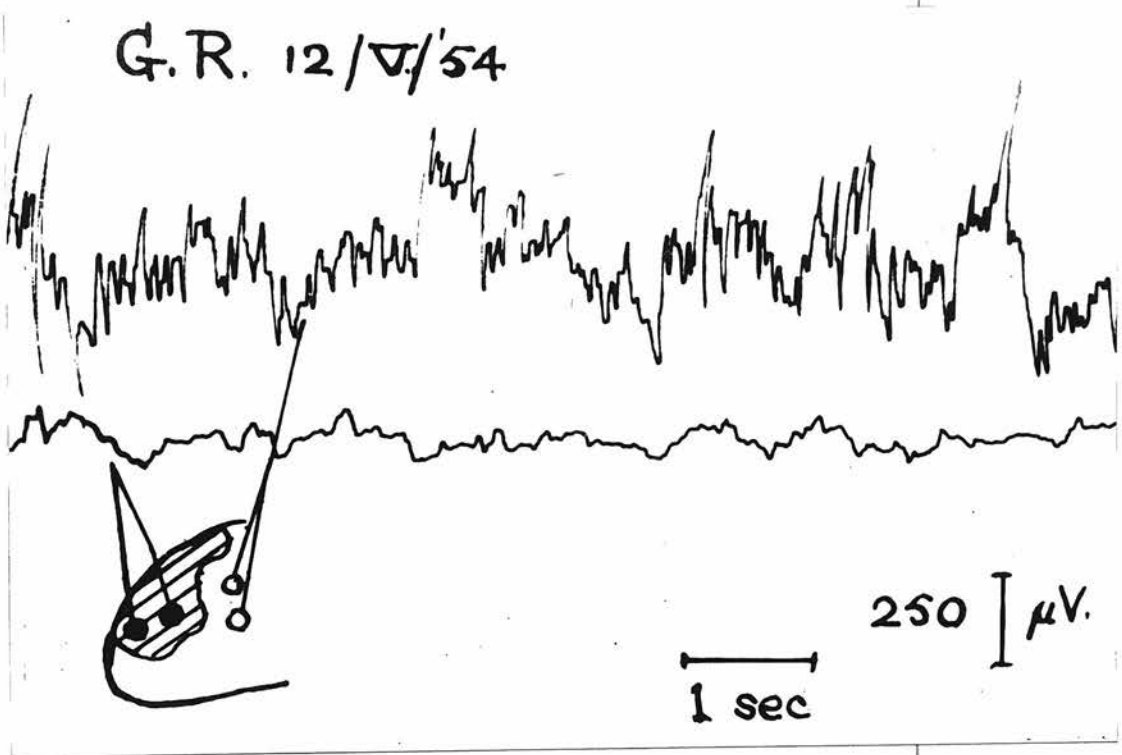


Fig.49

It is of interest that once again the same phenomena were repeated at electrocorticography in Case III. yet calcification within the cortex in that case was minimal. The tracing was rather less damped than in the first two cases. (Fig.49). Dr.Grey Walter reported: "from the region of the vascular abnormality there were very few regular potentials and the maximum potential with electrodes about 2 cm. apart was 100 - 200 microvolts in occasional slow waves. This contrasted with the activity beyond the margin of the naevus where the potentials frequently reached 500 microvolts, and a wide variety of abnormal wave-forms was present throughout".

Tracings from a small localised angiomatose area on the temporal lobe with rather more sparsely arranged venules than elsewhere, showed only irregular high voltage discharges characteristic of the rest of the non-angiomatose cortex.

The observations in Case IV. were in one respect parallel to the previous ones, in that the slow high-voltage discharges which were recorded at the surface everywhere were evidently superficial, because at a depth of 2 cm. and more away from the cerebral surface, the voltages were reduced to about a quarter of those at a depth of 1 cm.

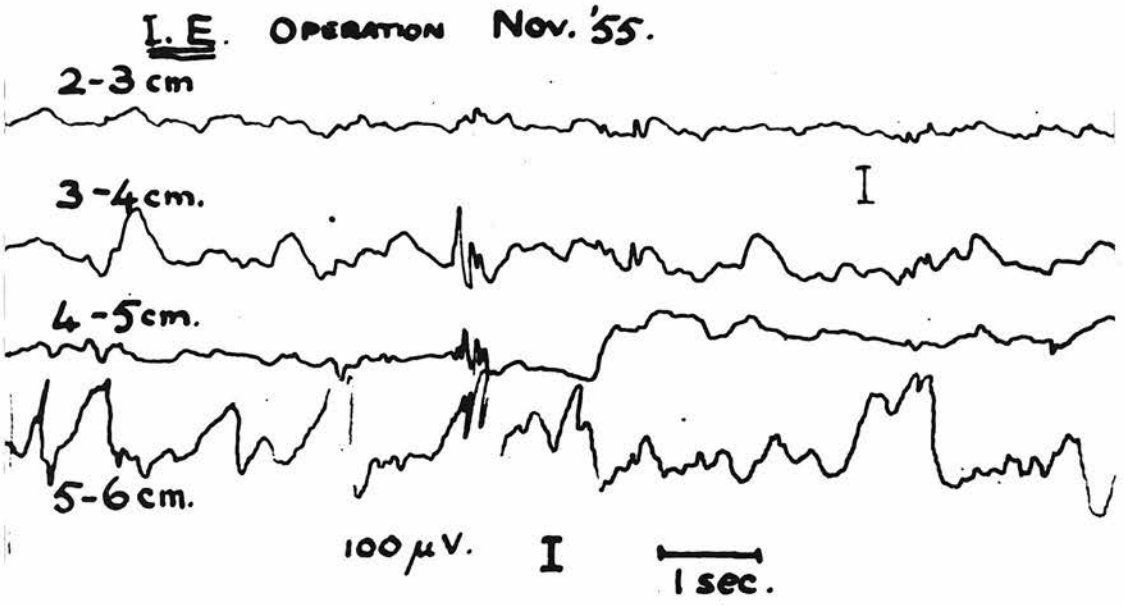
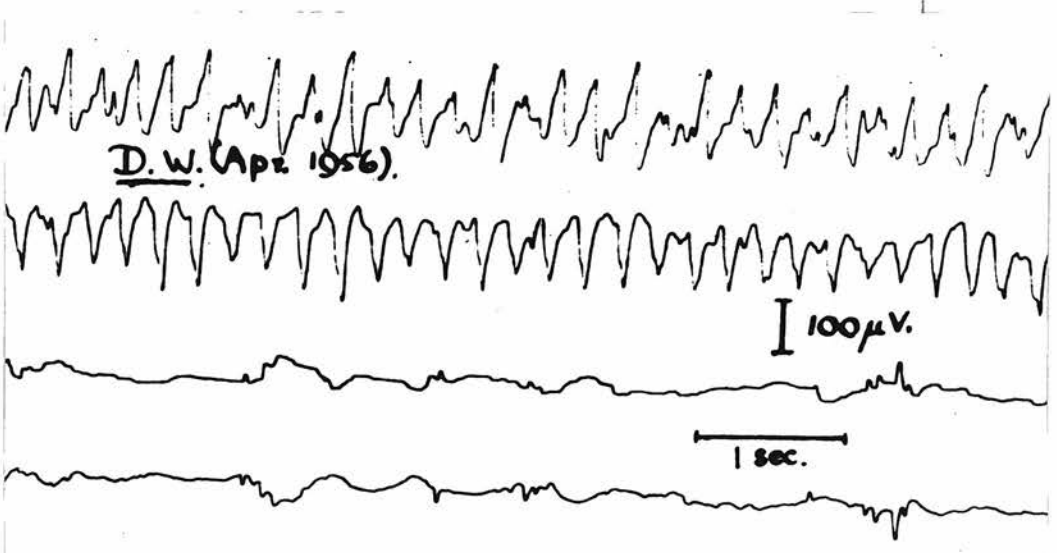


Fig.50

Finally, the tracings of Case V. introduced a novel feature which further experience may show is related to the age of the subject (1 year). This concerns very high voltage 7 c/s. waves in long regular trains which were obtained only from the subcortex at several samplings near the occipital pole. Tracings of this type were new in Dr.Grey Walter's considerable experience, and he was unable to ascribe a particular significance to them.



The recordings from the cerebral surface in this patient were characterised by very large slow delta activity, the amplitude being greatest posteriorly and superiorly. No focus or "silent" area was observed.

It remains only in this Section to present the noteworthy electroencephalogram in Case I. 19 days after the cerebral resection (Fig.52).

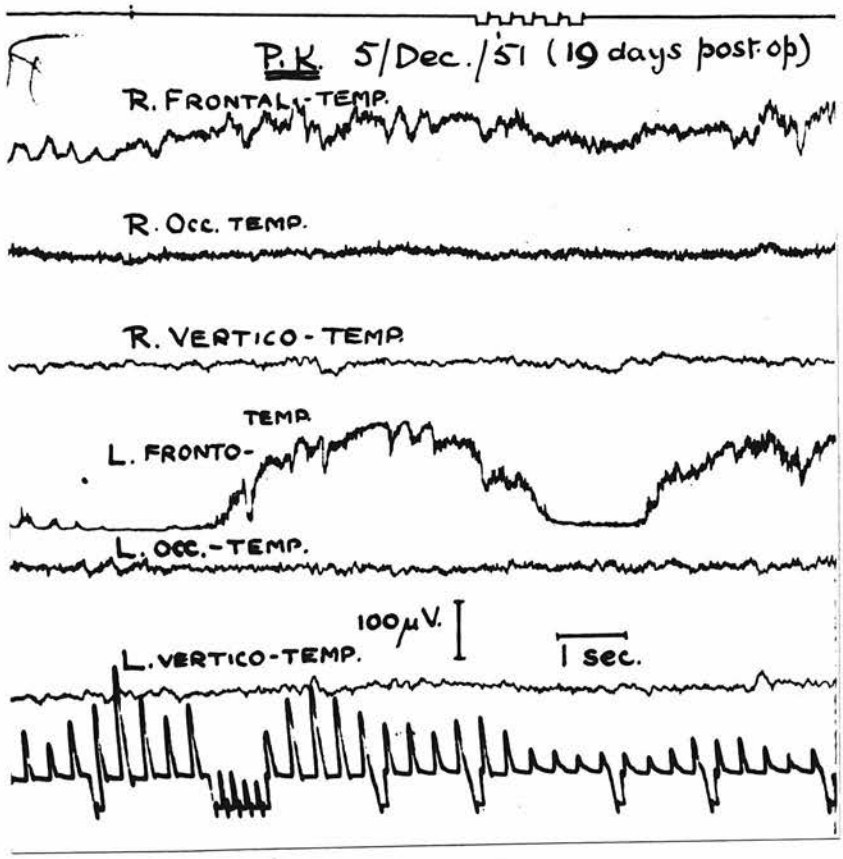


Fig.52

The tracings from ALL areas are vastly improved. Subsequent examinations have yielded virtually normal records, and latterly even without the beneficent effect of anti-convulsant drugs.

Electrocortical activity is decreased by hypoxia, and by excess of carbon dioxide in the circulating blood - as when breathing 10% CO_2 in oxygen (Adrian and Matthews, 1934; Lennox, Gibbs and Gibbs, 1936).

Wilson (1957) has described the virtual obliteration of potential variations in the electroencephalogram in anaesthetised man if one bronchus is clamped during pneumonectomy. This manoeuvre is equivalent to a veno-arterial shunt and causes approximately a 50% increase in carbon dioxide tension in the circulating blood. The oxygen tension falls, but very far short of the level of hypoxia necessary to produce a comparable effect on the electroencephalogram. This observation suggests that increase of carbon dioxide tension in the blood is more potent than a fall of oxygen tension in bringing about electrocortical inactivity.

When opportunity again presents an attempt will be made to obtain direct evidence of these gaseous tensions in the cerebral tissues underlying the vascular anomaly.

There is as yet no literature on this detail of the syndrome. Probably these are the first cases in which electrical tracings have been made at operation. Obrador (1954) arranged for electrocorticography but he had the misfortune of technical difficulties with his equipment during the operation.

HISTOLOGICAL FINDINGS

The new contributions are, (1) the histological findings in a young subject; and, (2) the demonstration of the abundant colloid matrix in which the calcific concretions are developed.

Carbol-azure (a Nissl type of stain), and von Kossa's stain was used to demonstrate calcium.

The periodic acid Schiff method (P.A.S.) was employed to reveal the colloid matrix in which calcium is subsequently deposited. This matrix was apparent at the site of concretions, after decalcification. This stain has an affinity for carbohydrate-containing proteins.

Holzer's stain was used to demonstrate fibrillary neuroglia, and the Gomori silver method for reticulin.

The Concretions

These were present in the cortex in all five cases studied. They were large and often contiguous in the molecular layer and outer part of the gray matter over wide areas in Cases I and II, and limited in extent in Cases III and IV. In Case I the largest concretions lay most superficially.

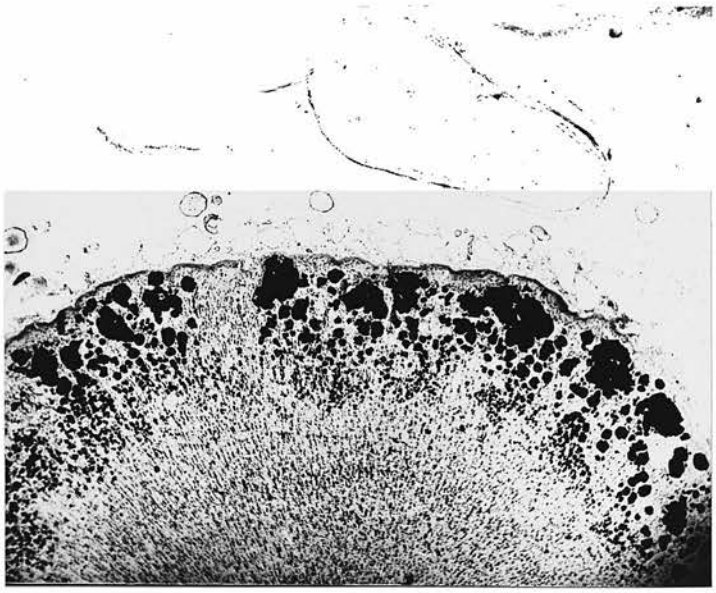


Fig.53. Case I. Cortical concretions. Carbol-azure stain.

In the less-calcified areas in Case II. there was a tendency for the deeper parts of gyri to be also involved, and this was seen also in the adjacent gyri in Case III.

In Case II one of the peristriate areas showed a bilaminar distribution of concretions (Fig.54), which is perhaps unique, in both the outer zone and the sixth layer.

Fig.54. Case II. Bilaminar array of concretions, showing the distribution in buried cortex in relation to the depths of a sulcus. Carbol-azure.

The concretions usually had a concentric laminated appearance, with as a rule a central core representing a former blood-vessel. This detail was well shown in the smaller concretions.

Small concretions were found scantily in the white matter, bearing no relation in degree to the density of calcification in the overlying cortex.

In general there was a tendency for the buried parts of the cortex, in relation to the depths of sulci, mainly to show the mineral deposits, the crowns of gyri being relatively spared.

Perivascular Calcification

The deposits always appeared like droplets on the outer surface of the smaller vessels, of pre-capillary order, in the outer zone of the cortex, usually in parts devoid of the larger concretions.

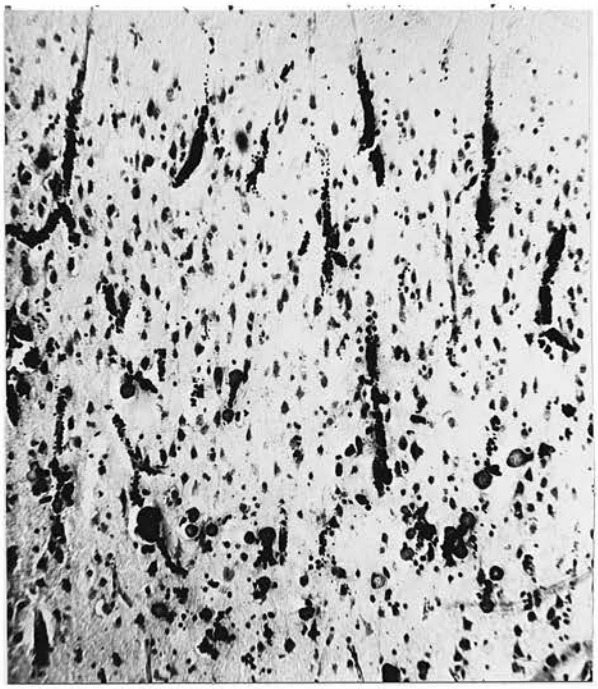


Fig.55. Case III. Perivascular calcification in the cortex. Carbol-azure.

In Cases III. and IV. this droplet incrustation of vessels also occurred in other laminae, especially in the fourth layer in the visuo-sensory area.

Until the material of Case V. came to hand we had assumed that perivascular incrustation would long precede the formation of concretions, an impression fostered by the frequent finding of perivascular calcification alone at the periphery of areas with many concretions. However, sparsely

distributed calcified deposits were seen in this case to be scattered throughout the cortex with no apparent laminar predilection, though with a somewhat greater concentration in relation to the depths of sulci. Further, small concretions were often seen in close relation to the wall of a vessel, but many were at a distance therefrom. In short, deposition of calcium on the smaller vessels in this Case V. had obviously not proceeded far.

The Colloid Matrix

This appears to be the precursor of calcification, providing a matrix which takes up calcium salts. The material from the infant (Case V.) was the most instructive of the series.

Whereas with the carbol-azure stain the dark blue calcifications were relatively scanty, a far greater abundance of abnormal, colloid deposit was seen in the P.A.S. preparations. The great majority of the deposits stained a bright pink, only a few staining a smooth purple colour with the haematoxylin counter-stain, indicating that calcification was already under way in those particular deposits.

The P.A.S.-positive deposits were roughly circular in outline, in sections, and showed a finely fibrillar structure, distinguishable from the ground-substance by the greater intensity of their pink staining. The relationship of these structures to blood vessels was clearly apparent.

In many instances they lay along the course of a visible pre-capillary (Fig.56). Often short lengths of blood vessel projected from them or were seen within them.

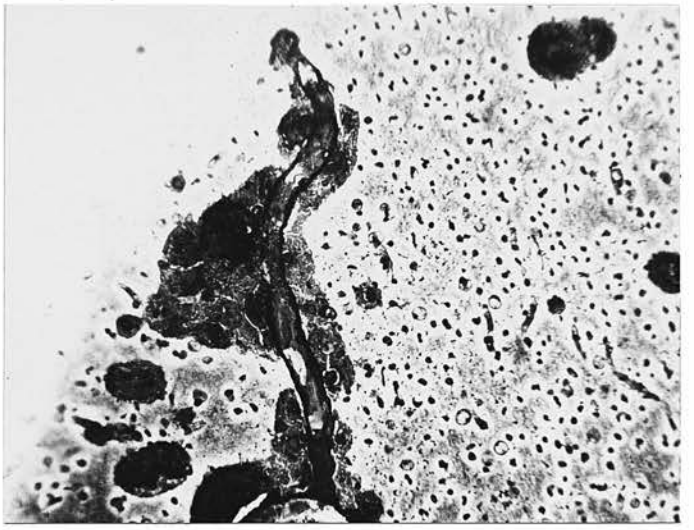


Fig.56. Case V. Perivascular colloid accretion. P.A.S. stain.

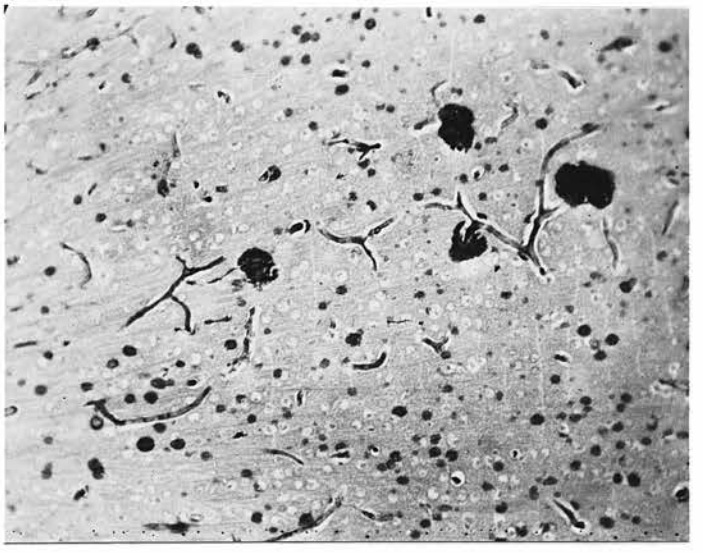


Fig.57. Case V. Colloid accretions in relation to vessels in the cortex. P.A.S. stain.

This pre-calcification material was also shown very well in reticulin preparations, which also confirmed its close proximity to blood vessels. Apart from these larger fibrillar masses,

numerous much smaller spherical deposits of similar type were seen with no observable relationship to cells or blood vessels.

As has been noted above the colloid matrix is revealed in the larger concretions with the P.A.S. method, after decalcification.

The Cortical Parenchyma

The presence of large concretions necessarily implies replacement of cortical substance by their bulk. Many of the larger concretions are surrounded by strands of neuroglia fibres. The tissue intervening between large concretions shows, however, a rather surprising degree of normality (Fig.58), and with little evidence of gliosis.

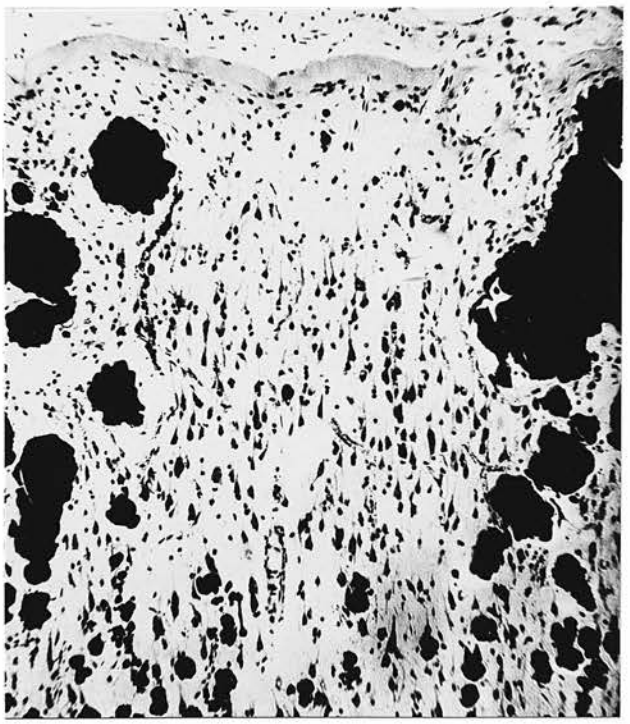


Fig.58. Case I. Surviving cortex between concretions. Carbol-azure.

In two alone of the cases (II. and IV.) small foci of severe atrophy of the cortex were found, where nerve cells had disappeared, save in portions of the deeper, and sometimes the most superficial layers of the cortex. Neuroglial nuclei were increased in number.

A heavy overgrowth of the adventitial coats of fibrotic vessels, connected by a dense network of reticulin fibres characterised these two cases, in some areas of the sections, particularly in cortex related to the depths of sulci.

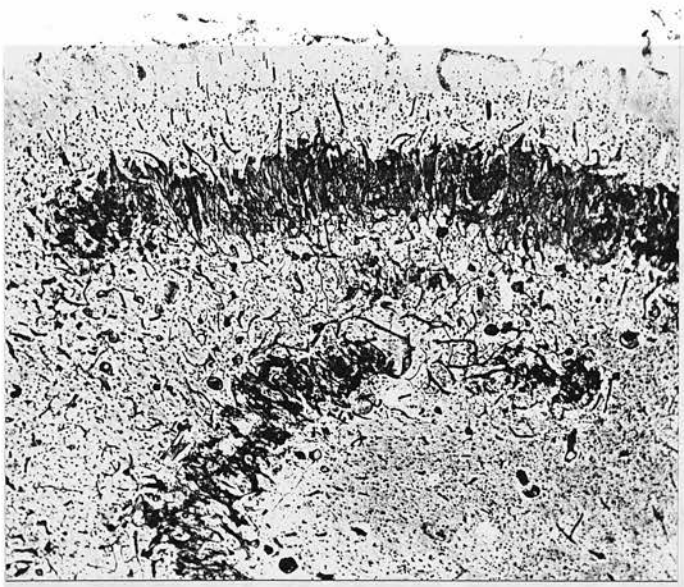


Fig.59. Case IV. Fibrotic vascular zone in cortex. Reticulin stain.

In Case IV. these foci were confluent, forming long strips in the cortex (Fig.59). In both cases these foci were usually the seat of a diffuse "powdery" calcification, without concretions, (Fig.60), but here and there non-calcified foci of this type were observed.

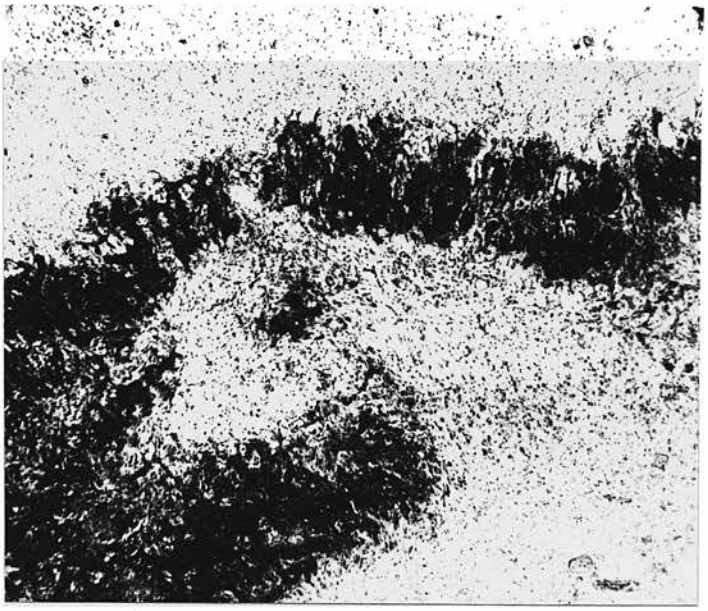


Fig.60. Case IV. Zone of diffuse calcification in cortex. Carbol-azure.

In Case II. a few calcified nerve cells were to be found in the neighbourhood of these foci, and in Case IV. extensive neuronal atrophy and gliosis extended out decreasingly from these areas of vascular fibrosis.

Meningeal Vessels

In general the angiomatose vessels in the meninges were small and of fairly uniform calibre. Their walls were thin and often contiguous. They dipped down into sulci.

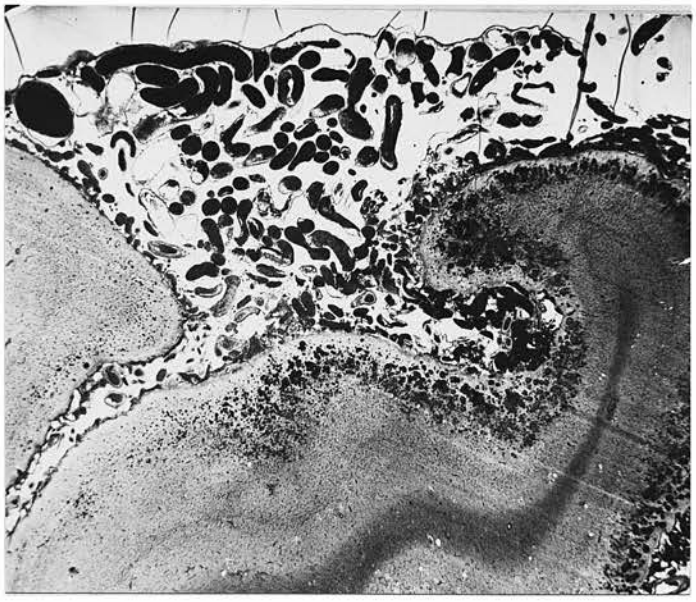


Fig.61. Case II. Angiomatose venules at the surface. Masson trichrome stain.

The feltwork of venules tended to be thickest overlying the areas of greatest cortical calcification, though that did not hold in Case II.

Calcification of adventitia, and sometimes of the media, of arteries in the abnormal area of meninges was seen in Cases I., II., and IV. This arterial calcification was absent in Case III. and in the infant (Case V.). In Case II. only this calcification was confined to meningeal arteries in the depths of sulci.

It remains now to add some further histological details noted in the material from the infant (Case V.).

A peculiar feature of this case was the presence of calcified branched cells, many obviously microglial in type, arranged in

conspicuously laminar formation in the fourth, and to a lesser extent in the sixth, layers of cortex (Figs. 62 and 63).

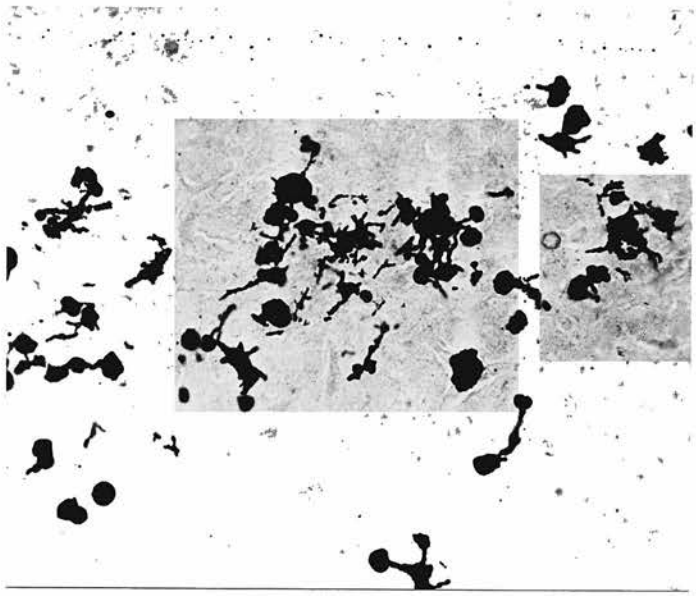


Fig.62. Case V. Calcified glial cells in cortex. von Kossa stain.

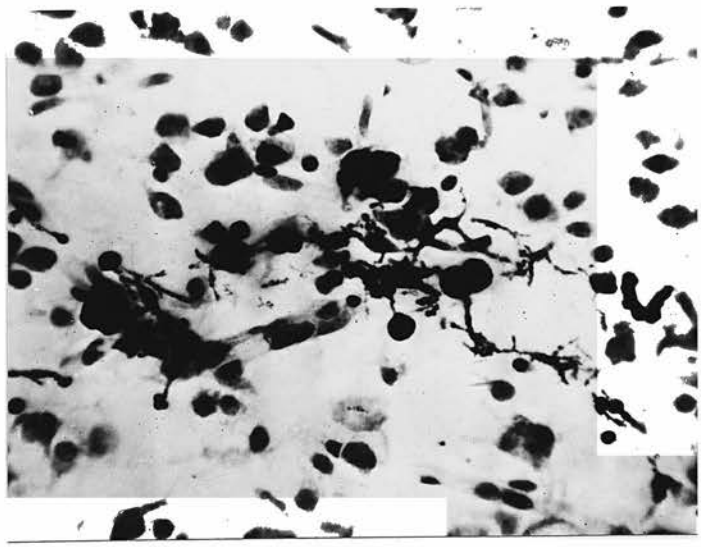


Fig.63. Case V. Calcified glial cells in cortex. Carbol-azure.

The processes of these cells often ended in small balls of calcified material. Although a few of the larger calcified cell-bodies had a roughly triangular shape, it was not possible to identify them with certainty as belonging to neurones.

The larger concretions in this case were usually of irregular mulberry shape, suggesting the fusion of separate globules. They showed no concentric lamination in their structure.

Discussion

There would appear to be a relationship between the degree of cyanosis of the angiomatose venules at the surface and the degree of cortical calcification underlying, in this series of cases. This suggests that local circulatory stasis may be an operative factor in the process. The occasional calcification of arteries, especially in the depths of a sulcus, suggests local hypoxia (Meyer, 1951).

The case of Bates (and Dr.Norman) seems to indicate that intracortical calcification occurs only where the vascular anomaly consists of surface vessels of small calibre.

The histological findings in the P.A.S. preparations at the age of one year (Case IV.) bring into evident relationship the smaller blood vessels and the masses of carbohydrate-containing substance, whether by leakage from the vessels or by precipitation in their vicinity. The fibrillar texture of these deposits suggests that the material - in solution or suspension - had been adsorbed by the finer glial fibrils of the ground-substance. Some of the microglia had also taken up this material and had become incrusted with

calcium.

The more numerous very small spherical masses of the P.A.S.-positive substance seen in certain areas may represent minimal capillary leakages, but this hypothesis cannot be verified since only a very few vessels were rendered visible by the ordinary staining methods employed.

The calcifying process of the vessels in the Sturge-Weber anomaly is similar to that found by other investigators in comparable states of cerebral calcification. Mallory (1896) showed that a transparent colloidal matrix remained after decalcification, and he postulated that this "colloid material" was the essential fore-runner of calcification in the brain. In the familial form of cerebral calcifications associated with microcephaly Jervis (1954) has demonstrated that this matrix is strongly stained by the P.A.S. method. The evidence from Case IV. shows very well that the colloidal material is abundantly present at a period in life prior to any extensive deposition of calcium.

Altered permeability of the vessel walls appears to be the most probable common pathogenetic factor in all forms of perivascular calcification. This factor is most obvious in inflammatory states, droplet incrustations identical with those seen in the Sturge-Weber condition being commonly found as a sequela of encephalitis. If it is postulated

that increased permeability of the cerebral vessels in the Sturge-Weber malady is due to some structural anomaly one is faced with the problem of accounting for the predominantly intracerebral location of the calcifications, while the obviously abnormal meningeal vessels escape. It seems more plausible to suppose that the presence of the meningeal angiomatosis leads to some degree of slowing of the circulation and stagnant hypoxia in the cortex, and hence to an increased permeability of the intracortical vessels.

The principal cause of neuronal destruction is the mechanical replacement by massive concretions. Comment has already been made on the persistence of areas with nerve cells of normal appearance between the calcified masses; it may well be that a diminished circulatory flow is able to sustain in a viable state the lesser remaining volume of neuronal cortex consequent on the presence of large concretions within it.

The minor degrees of intracortical vascular calcification do not appear to damage the cortex in any way.

Turning now to Case IV., the sections provide an explanation for the scattered faint and quite atypical radiological shadows of the calcifications in that case. The calcific deposits in the laminar strips of vascular fibrosis and marked overgrowth of connective tissue and reticulin, were numerous

but finely-divided: there were no concretions in these areas and consequently no gyriform double-countoured patterns were visible radiologically.

COMMENTS ON THE LITERATURE

Nearly 300 papers containing descriptions of 382 cases have been studied. 19 references have not been obtainable in the British medical libraries in the original or as a photostat copy. The material surveyed, however, permits some statistical approximations and includes all of the more important papers.

For several reasons many of the described cases cannot be accepted as undoubted examples of the Sturge-Weber anomaly. In the earliest reports radiological information was necessarily lacking, so that unless post-mortem confirmation of the diagnosis was to hand, those early cases have been excluded from consideration, with the exception of Sturge's case - and here sentiment and historical interest must be pleaded.

Some references proved to be no more than synopses of a few lines only, in reports of Society meetings, and have had to be discarded.

In quite a large group, comprising 186 cases, a facial naevus was present, but the neurological syndrome was slight or atypical and there was no radiological evidence or proof by operation that the brain harboured the characteristic vascular anomaly.

In another group of 26 cases with a facial naevus the intracranial lesion was clearly a

racemose intracerebral angioma, and of these many were of the arterialised variety. Episodes of massive intracranial haemorrhage brought some of those patients to clinical notice, and were misleading to a few of the earlier writers who inferred that intracranial haemorrhage could be a feature of the Sturge-Weber syndrome.

Quite a large number of reports in the ophthalmological literature contain information which is clinically and radiologically too scanty for inclusion of the cases in the Sturge-Weber group. Passing comment must be made on the considerable number of reports in which there is no reference to the visual fields (even in some ophthalmological papers) or they are said to be normal, yet one occipital lobe has been the seat of extensive and dense calcification implicating the striate area. The explanation must lie in the assumption that the presence of a gross homonymous hemianopia cannot be established in infants or in the feeble-minded, which is of course untrue. Furtado (1936) comments on the curious lack of recorded field defects in the literature. A homonymous hemianopia was found in six of the seven personal cases.

The criteria which serve to identify the Sturge-Weber malady are a facial naevus (evidently with a particular characteristic in its distribution), epilepsy, gyriform calcifications visible

radiologically within the cranial chamber (except in infancy), angiomatosis at the cerebral surface revealed at operation or post mortem examination, and perhaps buphthalmos or glaucoma.

This broad statement requires qualification however. Eight authors have described cases without a facial naevus which would otherwise be acceptable cases; as there was no naevus there was of course no glaucoma or buphthalmos: (Olivecrona et al., Cases 1 and 5, 1936; Esser, 1941; Longo, 1949; Lund, Cases 5 and 6, 1949; Snellman, Case 2, 1949; Chiro and Lindgren, Case 10, 1951; Popp-Vogt, 1951; and Livingston et al. 1956). These are cases of cerebral angiomatosis, and by definition are to be excluded from the Sturge-Weber category, though their close relationship is apparent. They suggest that the embryonic vascular maldevelopment (hypothetical persistence of the primordial plexus) can be determined after the vascular anlage has separated into layers for the skin and for the meninges; and that it is possible for the vasculature of the external layer to develop independently in a normal manner.

The Calcifications

It is abundantly evident from the literature that cortical calcification cannot be discerned radiologically in the first year or two of life, and therefore this evidence of the existence of the intracranial lesion is necessarily lacking in the 30 reports of cases below the age of 2 years.

Sommer and Demoullin (1947) saw no calcification in their case at the age of 2 years, but an extensive occipito, parieto-frontal deposit had appeared by the age of 8 years. Anderson (1945) reported negative films at 6 months, and "flecks" in one occipital lobe at 7 years, which had increased "several-fold" three years later. Worster-Drought (1948) saw no calcifications at 8 months but they were evident in both occipital lobes at 19 months. Kluska's case 3 (1947) showed quite marked calcification at the age of 7 years, increasing up to the time of the report, at the age of 12 years. Krabbe and Wissing's case (1929) remained radiologically stationary from the ages of 16 to 23 years. Similarly, McCoy and Voris (1948) saw no change over the interval from ages 13 to 20 years.

Some increase in extent and density of the scanty calcification was seen between the ages of 14 and 18 years in personal Case III.

The exact age at which the calcifications become radiologically detectable is not of academic

moment in the light of personal case V. with early calcification already present in microscopic sections of the brain at the age of 1 year.

The literature is understandably silent about the age at which pericapillary deposits begin to appear histologically, or even whether they are present at birth.

A further consideration with regard to the literature is that the earliest evidence of cortical calcification in X-ray films may well escape observation unless stereoscopic views of the skull are studied closely. The first of the series of films in Case VI. was reported normal.

Topography of the Facial and Cerebral Lesions.

The extension forwards of the calcification into the frontal lobe, comparable to that observed in the personal Case VII., is no rarity. Ten similar cases have been found (Rønne, 1937; Nussey and Miller, 1939; Hemblein, Prendergass and Widemann, 1940; Koch, 1940; de Gispert Cruz, Case 1, 1942; Kluska, Case 3, 1947; Sommer and Demoullin, 1947; Rodriguez and Canbarrere, 1950; Lichtenstein, 1954; Rullan and Rifkinson, 1954).

In a survey which omits many of the reported "acceptable" cases, Kautzky (1949) has inferred that an occipital location of the angiomatosis and calcifications can be expected when the first

division trigeminal field of the face exhibits the naevus; the second division field corresponds to a parietal location; and when all three division fields bear the naevus, the cerebral lesion extends forwards to the frontal lobe. While this last is true in the personal Case VII., and in most of the descriptions cited in the preceding paragraph, Rønne's patient had a naevus extending only over the forehead, eyelids and side of nose. The third division field was spared in the case of Sommer and Demoullin. The naevus in personal Case III. was in the first division field but the angiomatosis was parietal in location. Further, in personal Case II. the cerebral lesion was sharply restricted to the occipital lobe yet the facial naevus was quite extensive.

The distance which in the great majority of cases separates the superficial and deep vascular anomalies in the Sturge-Weber condition is striking. The implications of this have already been discussed (section on Embryological Considerations). Reference was there made to the almost unbroken rule that the naevus implicates the supra-ocular part of the face. Rønne (1937) and Kautzky (1949) have drawn attention to this association. One single exception has been found in the case of Neimann, Pierson and Manciaux (1953) concerning a boy aged 6 years with a naevus confined to the cheek, upper lip, temple and ear. A perfectly

typical gyriform occipital calcification was was displayed radiologically. No arteriograms or direct information as to the state of the brain were available, nevertheless this case must be included in the Sturge-Weber group. Occipital angioma with gyriform calcifications seems to be very rare indeed, and apart from the case of Furtado (1936), in the other examples of angioma with gyriform calcification the lesion was Sylvian or Rolandic in site.

This single case of Neimann, Pierson and Manciaux must prevent outright acceptance of the proposition that in the Sturge-Weber condition the naevus must necessarily implicate the upper eyelid or forehead, though it is otherwise invariably true in the reports surveyed.

It is doubtful whether angiomatosis comparable to that seen in Sturge-Weber cases ever occurs on the spinal cord. Frank angioma on and within the cord is familiar. At the other extreme, the so-called angiomatosis of the cord consists of an open network of small arteries and veins, visible in areas on the surface of the cord exposed at operation. No information is to hand whether the abnormal vessels lie only at pia-arachnoidal level. Indeed those small lesions might well pass unnoticed at post mortem examination with the vessels empty.

The degree of neurological disturbance

associated with angiomatosis of the cord, though often moderate, suggests that the vascular anomaly is not exclusively superficial. The vascular anomaly on the cord is always a very open network and does not convey the impression of a vascular stasis at the surface, in contrast to the cerebral angiomatosis of Sturge-Weber type.

In discussions about the trigeminal and cerebral topographical relationship in the Sturge-Weber anomaly, many writers have cited the cases of Cobb (1915) and Jefferson (Wyburn Mason, 1943; Case 42) describing cases of angioma of the spinal cord with cutaneous naevi in corresponding metameres. Such rare cases are however homologous with cerebral angioma associated with facial naevus, and have no direct bearing on the Sturge-Weber anomaly.

Sex Incidence and Side Affected.

Superficially this is not remarkable. Males comprised 51% of the acceptable cases in the literature surveyed. The left side was affected in 48%. In the very few with a bilateral facial naevus but evidence of cerebral angiomatosis on one side, that side was considered the affected one.

When the side affected was considered in relation to the sex a curious trend emerged, the

males showing a bias for affection of the left, and the females for affection of the right side. In a few of the reports the sex or the side affected was not specified, and those cases were of course discarded. Including the seven personal cases the figures were:

Males.	Left side, 45.	Right side, 35.
Females.	Right side, 50.	Left side, 32.

This was an unanticipated finding and emerged after the whole case material had been annotated, so that there can be no question of subconscious bias in the estimation.

Applying the χ^2 test the figures are significant to the 5% level.

Bilateral occipital gyriform calcifications were reported by Worster-Drought (1948) in his case with a naevus involving the whole face and elsewhere. In the Case 9 of Chiro and Lindgren (1951) both occipital lobes had the typical calcifications but there was no facial naevus: this record omits mention of the state of the patient's vision. Paarnitzke's case (1956) with symmetrical occipital calcification, resembling that seen in basal ganglia and without a clear gyriform pattern, had no facial naevus and the one occipital lobe resected showed no angiomatosis. There was no epilepsy. This case cannot be accepted as belonging to the Sturge-Weber category.

Epilepsy.

Epilepsy has occurred in every reported case where the essential components of the Sturge-Weber syndrome have been present. This fact is noteworthy, and unique among potentially epileptogenic lesions.

The onset of epilepsy has usually been within the first two years of life. Epilepsy beginning in later childhood or adult life is characteristic of cerebral angioma. The literature surveyed has many examples.

In the group of "acceptable" cases there are recurring accounts of a pyrexial illness heralding an initial burst of epileptic attacks. No information throwing light on this phenomenon is to hand; the history is usually given by parents in retrospect. Another curious feature is a relative or complete remission for several years, usually after some considerable period of liability to attacks, after which the attacks return in accentuated form and with increasing persistence. The cases of Olivecrona (No.4) and Thayer (1955) are remarkable in the long gap of 20 or 30 years between the epilepsy in early childhood and its recurrence.

The reports tend to be disappointingly silent about the possibility of the remission being due to the effect of anti-convulsants. So often the

authors give a rather condensed clinical account in order to expand on the pathological, ophthalmological or other aspects of the case, and on discussion.

As might be expected, the attacks are predominantly of focal character or onset. The absence of a visual aura in the accounts, with such a preponderance of parieto-occipital lesions, is noteworthy. Blum and Mutrux (1949) alone record an aura of scintillating scotomata in the appropriate half-fields of vision. It must be remembered however that very many of the patients are intellectually retarded and might not volunteer a description of an aura.

Epilepsy declares itself predominantly in the first year of life, and by inference before any substantial deposit of mineral salts has had time to accumulate in the cortex. Thus the presence of these deposits cannot be invoked as a cause of the epilepsy, as has been suggested by Moniz and Lima (1935) and others.

On the other hand, the epilepsy is rarely neonatal in onset, and when the liability to attacks first declares itself, it is apt to do so abruptly and in no uncertain manner.

Cerebellar and Pontine Atrophy.

Cushing (1906) was intrigued by the neurological implications of the contralateral cerebellar atrophy in his first case. Volland (1912, Case 1) and van der Hoeve (1936) had similar findings to report. Schmidt (1952) observed ipsilateral and pontine atrophy, and Wohlwill and Yakovliev (1957), reporting the post mortem findings in the Case 14 of Yakovliev and Guthrie (1931), recorded bilateral cerebellar atrophy.

It is to be remembered that the angiomatosis is not found on the surface of the cerebellum or brain stem, and the mechanism whereby this low-level atrophic state arises must remain a matter of speculation. It is however one piece of evidence showing that the vascular anomaly is not alone responsible for the wider neurological disturbances shown by nearly all patients with the Sturge-Weber condition. Danis and v.Bogaert (1951) have described a case with "crossed" cerebellar atrophy and abnormal vascularity on the surface of that hemisphere and corresponding half of the pons, but their excellent figures do not reveal an angiomatosis of the Sturge-Weber type there, although one cerebral hemisphere is typical (with angiomatosis extending anteriorly on the tuber cinereum and bordering on the chiasm): the patient had a facial naevus. (By kind co-operation of Dr.v. Bogaert this brain was made available in Brussels

at a recent Congress and a corroborative personal inspection of the cerebellum was made possible).

The incidence of cerebellar atrophy cannot accurately be determined because so many of the reports are purely clinical. Cushing recorded no clinical abnormalities of cerebellar type in his patient at the age of 4 years. It may be that a degree of cerebellar maldevelopment in these cases can pass undetected clinically. Bilateral cerebellar disease is strongly suspected in personal Case VII., a young adult. Post mortem examinations were carried out in 21 of the acceptable cases reviewed in this Thesis, and the above six reports record atrophy of the cerebellum or brain stem.

Circulation in the Angiomatose Areas.

The circulation in the angiomatose venules of Sturge-Weber type appears to be very sluggish, as judged by the degree of oxygen-reduction of the blood circulating within them. In the personal cases no directional flow of the venous blood could be established at operation by the rough method of blanching with digital pressure.

Moniz and Lima (1935) seem to have been the first to investigate the cerebral circulation by carotid angiography in the Sturge-Weber malady. They found a retardation of both arterial and

venous phases of filling on the affected side: their figure shows that the carotid artery was certainly not in spasm. Cerebral veins were still apparent at 4.5 seconds. No vessels were visualised in the area of gyriform calcification. The angiograms were normal on the unaffected side. Furtado (1936) observed a local retardation of the circulation, but his figures and description of the angiograms suggest that he may have been dealing with a partly arterialised angioma, albeit his case had "cerebriform" occipital calcifications.

Green (1945) noted delayed arterial filling in the affected region, and this has been confirmed by later writers.

It is probable that the stasis is peripheral, at cortical level.

In connection with epilepsy in relation to the cerebral circulation in these cases a parallel can be drawn between the effects of experimental ligation of a coronary artery of the heart (Beck, 1935) and the circulatory state postulated in the angiomatose area of the cerebrum. Beck and his team have shown that a focal anoxaemia is of particular danger to the heart. When a major coronary branch is ligated its territory of supply rapidly becomes cyanotic. A cardiac dysrhythmia and electrocardiographic instability almost at once ensues and the heart goes into ventricular fibrillation. In contrast the heart remains stable

and continues to function effectively in advanced anoxia, provided the anoxia is of uniform degree throughout the myocardium. In the Sturge-Weber condition we have a postulated, and very probable, territorial hypoxia. If a danger to the functional stability of the brain may exist from the juxtaposition of hypoxic and normal circulatory conditions, the undoubted benefit accruing from removal of a pathological and electrically-inert lobe of the brain ceases to be a paradox.

The Intraocular Hypertension.

Either buphthalmos or glaucoma has been reported in a minority of cases. Taking the 170 surveyed acceptable cases of the Sturge-Weber condition as a basis, buphthalmos was mentioned in 14% and glaucoma in 8% of the reports. This survey has revealed no characteristics in the distribution of the naevus which seem to be obligatorily linked with the occurrence of intraocular hypertension, either before or after birth. In general the forehead, eyelids and cheek show the facial naevus, and O'Brien and Porter (1933) would have that distribution as a pre-requisite.

Cases have been reported in the ophthalmological literature, however, of bilateral naevus with buphthalmos on one side and a normal eye on the other.

Woringer's case (1954) and that of Duhamel and Goetz (1954) showed buphthalmos only on the side opposite to the naevus. Danis and v.Bogaert (1951) described the post mortem findings of a case in which the eyes had been repeatedly examined during life and found normal, and the ocular tension had never been raised, yet sections of the globe on the side of a facial naevus disclosed an extensive choroidal angioma, maximal in the vicinity of the optic disc.

Further, Ballantyne (1930) draws attention to

the 15 reports up to that time of buphthalmos or glaucoma in association with plexiform neuroma of the face and eyelids; ciliary nerves were found to be neuromatous but investigation of the bulbus oculi gave no clue to the mechanism of the intra-ocular hypertension.

The state of knowledge regarding the cause of buphthalmos or glaucoma in the Sturge-Weber cases appears to be unsatisfactory and there is to date no agreed view as to the aetiology. The findings in the many eyeballs examined histologically have been disappointingly inconsistent.

Angiomatosis of the choroid was found by Milles (1884), Snell (1886), Stoewer (1908) de Haas, and Craig (1949). "Angioma" of the choroid was seen with the ophthalmoscope by Lawford (1895) and by O'Brien and Porter (1933) and "dilated retinal vessels" were reported by Nakamura (1922), Krause (1929) and Tyson (1932). Knapp (1928) found angiomatosis of the iris.

In Safar's case (1923) the canal of Schlemm was narrowed and displaced backward, the chamber angle being covered by a web of connective tissue. On the other hand Clausen (1926), Parkes Weber (1929) and Craig (1949) found neither vascular abnormalities nor obstruction of the angle of the anterior chamber.

Beftman (1904) thought that engorgement of thin walled veins in the choroid encouraged excessive transudation of fluid, and that the absorption of

aqueous was diminished. Elschnig (1918) also invoked a plethoric condition of the choroidal vessels, a hypothesis which he considered gained support from the temporary lowering of intraocular tension caused by carotid compression. Freese (1920) suggested interference with the sympathetic nerve supply. Cabannes (1909) ascribed the buphthalmos to a local gigantism of the angiomatose soft tissues; but one must object that the sclerotic is thinner than normal in those buphthalmic globes. Hudelo's postulate (1929) of a retarded escape of venous blood from the cavernous sinus owing to the existence of the intracranial angiomatosis, is not attractive.

Ballantyne (1930) in his review points out that secondary glaucoma is seen with retinal angioma, with or without retinal detachment or haemorrhage; it is the result of those gross lesions, and that primary glaucoma is seen in the Sturge-Weber condition. He also defines pseudo glaucoma as existing when, in the presence of angiomatosis of the conjunctiva perhaps, the cornea is wider than normal and the optic disc is excavated, but the ocular tension is normal.

There seems to be general agreement that buphthalmos is due to ante-natal rise of tension within the globe. Ballantyne concludes that there must be some embryonic fault because in some cases there are also other congenital ocular abnormalities,

such as deformity of the lens or coloboma of the iris. No theory fits all cases.

One of Larmande's two genuine Sturge-Weber cases is remarkable in that calcification was evident radiologically in the angiomatose choroid of a buphthalmic eye. It must be pointed out that this is an exceptional circumstance because calcification seems to be rare in the globes which have been examined after removal. Bentsen, Dalsgaard-Nielsen and Moller (1938) found calcification in a glaucomatous eye in their Case 3, which however had no epilepsy up to the age of 6 years and the brain showed no calcification radiologically. This is a questionable Sturge-Weber case.

Surgical Treatment.

The earliest reported operation is that of Cushing (1906, Case 2). He exposed the frontal lobe by osteoplastic craniotomy and as a preliminary ligated the external carotid artery; this, he observed, promptly caused the facial naevus to become "whiter". Large dural veins were found in the anterior two thirds of the exposed dura mater, corresponding to the area of the naevus in the forehead and scalp. No cerebral vascular abnormality was apparent at this anterior exploration. The patient had a naevus confined to the first division

trigeminal field and it is highly probable that the vascular anomaly lay posteriorly. In an earlier case, which he also reports, he abandoned a frontal exploration after making one trephine hole because of excessive haemorrhage. The patient died some time later and at post mortem examination the meninges of the whole of the cerebral hemisphere on the side of the naevus showed a diffuse vascularity. The cerebral and cerebellar hemispheres on the side opposite to the facial naevus were smaller than their fellows: the ipsilateral trigeminal ganglion was atrophic.

With this first case of Cushing was born the legend of the dangerous operative risk which cases of the Sturge-Weber syndrome would present, an argument still being adduced in support of radio-therapy as the line of treatment to be preferred.

Olivecrona (1936) was the first to expose the occipital lesion and resect it, (Cases 1 and 5) with benefit to the patient. Dimitri and Balado (1933), Della Torre (1934) and Tonnis (1936) had exposed the occipital lesion and applied diathermy coagulation to parts of the pathological area. Lobectomies have since been reported, with encouraging results, by Bentsen, Dalsgaard-Nielsen and Moller (1938 - Busch operated), Bentzen (1947), Snellman (1945), Green, Foster and Berens (1950), Obrador (1954), and others.

Broager and Hertz (1949) and Huber and Zweymuller (1954) explored the Rolandic region in their cases, guided by abnormal electroencephalographic foci, and found epileptogenic lesions other than angiomatosis. Pinto-Pupo (1953) thinks occipital lobectomy is illogical because the greatest E.E.G. abnormalities are elsewhere in the hemisphere.

The authors who have performed occipital lobectomy all report improved medicinal control of the fits, and in many instances a cessation of attacks in the relatively short periods of post-operative observation up to the time of publication.

Nosography and Pathology.

There is considerable discussion and much cross-quotation in the literature concerning the mode of origin, and relationship to other conditions, of the Sturge-Weber malady. It would be true to state that none of it contributes to a better understanding of the intimate cause of this congenital anomaly or of its distribution in individual cases.

One could gain the impression from the literature, and particularly from the neurological literature, that the head is a site of predilection

for capillary naevi; but that could be a false deduction because it is the associated anomalies in the brain which bring the patient to clinical notice. Subjects with vascular naevi of the limbs and trunk may abound in proportion, but their malady is cosmetic, they are not seriously incommoded as is the epileptic, and their cases are not recorded as clinical "specimens". Moreover they have none of the intriguing interest of a coincident superficial and deep embryological maldevelopment of tissues.

Bergstrand (1936) gives an authoritative account of the vascular anomalies and tumours of the brain and follows Virchow's classification, as follows:

1. Angioma cavernosum. The walls of vessels pertain to more than one lumen.

2. Angioma racemosum. Each vessel is a separate entity and the tangle of vessels is separated by some other tissue.

   (a) Telangiectasia
   (b) Sturge-Weber disease (added by Bergstrand)
   (c) Angioma arteriale
   (d) Angioma racemosum venosum
   (e) Aneurysma arterio-venosum

3. Angioreticuloma (Roussy and Oberling), vel angioblastoma, vel Lindau tumour.

4. Angioglioma.

Bergstrand truly remarks that he cannot "straightly correlate" these conditions clinically. In discussion on this paper Lindau preferred the term haemangioblastoma, as directing attention more truly, i.e. away from the haemopoietic system.

Good evidence of a hereditary disposition is conspicuously lacking in spite of many statements to the contrary. Koch (1940) makes much of his observations of one large family in which some collaterals and antecedents had migraine, epilepsy or mental deficiency. Very occasionally in the literature a parent or grandparent is reported as having had a vascular naevus of the trunk or limbs, but that incidence could perhaps be no more than that of naevus in the general population.

No author has discovered the Sturge-Weber anomaly in siblings, or two examples in one family and their relatives. Consanguinity of parents has never been noted.

Two cases in negresses were described by Cohen and Kay (1941) and by Henblein, Prendergass and Widmann (1940), and these are the only well-studied examples in coloured subjects in the literature surveyed. Soejoenses (1941) reported a possible case in a Javanese boy, but he had no radiological facilities and in other respects the account was incomplete. There are several Japanese papers which have not been obtainable, presumably describing cases in Orientals. It would indeed be surprising were the Sturge-Weber malady confined to the white races. It is safe to assume that cases occurring in the white races are much more likely to be worked up and published.

Van der Hoeve (1936) made a plea for the Sturge-Weber disease to be included in the phakomatoses - a "fourth phakomatosis", the others being von Recklinghausen's neurofibromatosis, Bourneville's tuberous sclerosis, and the von Hippel-Lindau cerebellar and retinal abnormalities. Phakomatosis means a state of tumour-like formations arising in association with birth-marks. Yakovliev and Guthrie, van Bogaert and others talk of neuro-ectodermoses to embrace the conditions showing cutaneous and neural anomalies. Kissel and Arnould (1954) argue that neurofibromatosis is the result of an ectodermal dysplasia, and Sturge-Weber and related diseases have a basis of mesodermal dysplasia.

Tenuous parallels are drawn by some authors in philosophical discussion. For instance the occurrence of glaucoma in neurofibromatosis and in the Sturge-Weber anomaly has for de Morsier and Francescatti (1937) a significance, and they cite also calcification in optic nerve tumour and in the retina as a link. Cafe-au-lait spots were present in their Sturge-Weber case, and in three others in the literature. Lichtenstein (1954) also comments on the occasional occurrence simultaneously of pigmented and vascular naevi; he invokes a disturbance at the neural crest, and infers from the trigeminal relationship of the facial naevi that dysplastic vascular mesenchyme may migrate from the crest along with the developing trigeminal

branches. This hypothesis is unconvincing: with one exception the rare pigmented naevi have been described at a distance from the vascular naevi.

Both Kalischer (1901) and Krabbe (1934) feel that the condition is due to a co-ordinated ectodermal and mesodermal maldevelopment. Peters and Tebelis (1937) and Schmidt (1952) think that the angiomatose malformation is not the cause of the cerebral maldevelopment, whereas Lichtenstein and Rosenberg (1936) and Kroll and Staemmler (1948) would have the vascular anomaly as primary and the changes in the brain secondary. This latter view is difficult to reconcile with the widespread cerebral functional deficiencies evident in most of the patients and the tissue sclerosis often extending far wide of the angiomatosis.

Yakovliev and Guthrie (1931), Manolesco (1937), Rotth (1929) and others believe the frequent greater pigmentation of the iris on the affected side indicates a sympathetic nervous influence in the genesis of the anomaly.

After a century one can add nothing precise to the statement of Luschka (1854), referring at that time of course to facial naevus with angioma cerebri, that the anomaly is due to a congenital abnormality of the embryonic capillary system, and that the naevi of the skin and brain probably result from

a sequestration of part of the embryonic capillary system.

SUMMARY AND CONCLUSIONS

The literature contains a rather motley collection of cases purporting to be examples of the Sturge-Weber anomaly, and it seems desirable now to advocate a more rigid definition of the criteria for diagnosis.

A facial naevus is essential and if that be lacking the case should be considered an example of cerebral angiomatosis, if evidence be to hand of the characteristic intracranial vascular anomaly. Some recorded cases have a facial naevus but the intracranial lesion is patently an angioma, or the calcifications are not characteristic, or there is no real information as to the nature of the intracranial lesion.

Epilepsy is not mentioned in very many of the reports, and in view of the prevalence of epilepsy in the cases showing the other essential features of the syndrome, such cases on that count alone are suspect. It is evident that many authors have tried to squeeze their cases into the Sturge-Weber category on flimsy evidence.

The essential features of the condition under discussion are a facial vascular naevus, calcifications in the cerebrum on the same side (except in the very young), a history of epilepsy, and perhaps glaucoma or buphthalmos. Mental retardation, pareses and hemianopia are very

common but not obligatory findings in establishing the diagnosis.

The usual distant separation of the cutaneous and cerebral vascular lesions presents no mystery in view of the proximity of the optic vesicle and occipital part of the primitive forebrain very early in embryonic development. From this also it is inferred that the anomaly is determined earlier than has heretofore been postulated.

It is here suggested that the Sturge-Weber anomaly may result from persistence of the primordial vascular plexus described by Streeter in his studies of the development of the vascular apparatus of the human brain. His work also provides a plausible explanation for the escape of the brain-stem and cerebellum from affection by the angiomatosis.

The distribution of the cephalic naevus appears to be a matter of chance although the areas of involvement commonly bear in parts some relation to the processes and fissures of the embryonic face. In this manner also a relationship to branches of trigeminal nerve distribution eventuates, but it is submitted that the relationship is fortuitous and irrelevant. The evidence for such an opinion consists of the usual lack of a truly median limit of the naevus in some part; and in a few cases the clear indication that the cleft between the globular

and lateral nasal processes of the embryo can constitute a boundary of the naevus in the upper lip of the patient.

The morbid anatomy, and the process of intracerebral calcification have been considered. The basic factor is concluded to be a sluggishness of the circulation in the tissues underlying the angiomatose formation. Hypoxia, and possibly more important, an increased carbon-dioxide tension in the cerebral tissues is inferred. The cyanotic state of the angiomatose venules has been observed at operation, and electrocorticograms provide supporting evidence. Direct information as to the gaseous tensions in the abnormal cortex may later be forthcoming.

A histological study has been made of the Sturge-Weber lesion at the age of one year, the first to be recorded at such an early age. The processes preceding calcification in the abnormal cerebral tissues are revealed in this valuable case. In another case a unique series of radiographs from the age of two years demonstrates the progressive laying down of calcium deposits in the cortex. From these cases and others in the literature it is deduced that the characteristic cerebral calcification becomes radiologically detectable at the earliest during the second year of life.

The conflicting reports in the literature concerning the chemical composition of the cerebral

concretions are examined, and new and accurate chemical analyses of material from the personal cases are quoted. The deposits consist almost entirely of calcium phosphate and carbonate. The iron content is small in spite of the strong Prussian blue reaction given by them, which has led some writers astray.

In well marked examples of the Sturge-Weber anomaly it is evident from a few references in the literature and from some of the personal observations that the electrocortical discharges are of low voltage over the calcified area of the hemisphere. Opportunity was taken to record potentials directly from the cortex, and deeply, in five cases, and in three of them a very gross damping of the tracings from the angiomatose area was demonstrated. These appear to be the first records of this type made, dating from six years ago.

Excess of carbon dioxide is known to be considerably more potent than lack of oxygen in reducing cortical potentials. The records obtained are considered to provide circumstantial evidence that an excessive carbon dioxide tension exists in the cortex, consequent on an impeded circulation within it. The transition from the area of low voltage and damped tracings was observed to occur at the margin of the angiomatose areas. The whole of each angiomatose area showed this relative electrical "silence".

A parallel can be drawn between the electrical dysrhythmia rapidly induced in the heart as a whole by experimental ligation of a branch of a coronary artery, and the dysrhythmia and epilepsy which occurs in every case of the Sturge-Weber condition. The heart will remarkably tolerate asphyxia provided it is generalised, and the brain also does not regularly respond to general asphyxia by epileptic discharge. In the heart experiment, and probably in the Sturge-Weber condition, there is a territorial impairment of the circulatory flow; in the latter it is submitted that the circulatory impediment occurs on the venous side of the capillary system.

A further similitude exists between the epileptogenic properties of lesions such as parasagittal meningioma and cerebral venous thrombosis in which the venous drainage of a territory of the hemisphere becomes compromised, and the circumstances envisaged in the Sturge-Weber anomaly.

There is however no justification for proposing that a local impediment to the cerebral venous drainage fully explains the syndrome of epilepsy in the Sturge-Weber condition because there is ample evidence of tissue sclerosis, atrophy or dysfunction extending far beyond the site of the angiomatosis, and the fits so commonly have clinically a focal origin distant from the vascular abnormality. In addition the pons and cerebellum have shown atrophy

in some recorded cases.

In the cases studied and surveyed there is a very high incidence of mental deficiency. How far this has been determined by years of epilepsy is not clear: the improvement over the years in the personal cases when fits have been lessened and the known deleterious effect of frequent epileptic attacks on intellectual capacity, leads to a strong personal conviction that lobectomy should be practised in infancy if the lesion is posteriorly situated in the hemisphere, as it is in the great majority of cases. In view of the 100% incidence of epilepsy in genuine cases there would seem no logic in waiting for fits to occur. Some of the histories recorded here and in the literature indicate the swiftness of damage to intellectual capacity when epilepsy first occurs. It is realised that parents and others would be difficult to convince of this logic; until cases subjected to lobectomy in infancy and with (presumed) obvious benefit accumulated, no evidence would exist to support a policy of early intervention.

It is noteworthy that the results of lobectomy have so far been reported soon after operation with emphasis on the benefit accruing in respect of epilepsy. Thus there is virtually no information about the slow intellectual improvement which some at least of those patients have probably been showing in the years following publication.

A case has been made out for an assumption that unless the supra-ocular part of the face shows the vascular naevus, angiomatosis of the Sturge-Weber type is not to be expected on the brain. This feature could be of service in selecting cases early for lobectomy. The procedure followed in Case V. would be applicable - performing a small posterior cranial exploration in the first instance and proceeding in sequence to a formal craniotomy and resection.

This question of intervention before a clear indication arises is obviously debatable; and even were early intervention acknowledged as right and proper, the rarity of the malady would interfere with putting the policy into practice.

It is clearly established that lobectomy - occipital, parietal, temporal in any combination - in so far as permissible without inflicting crippling disability, is a very substantial contribution to the successful medicinal control or abolition of the epileptic attacks.

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A neurosurgical colleague, Mr.D.G.Phillips, kindly transferred the patient (Case III.) for study and treatment. A paediatrician, Dr.Jolly of Plymouth, referred Case II., knowing of my interest. Dr.N.S.Alcock of Exeter informed me about his former patient (Case VI.) and loaned his earlier X-ray films of the series, and Dr.St.J.Elkington of London allowed me to examine the patient, then under his care. Mr.Angell James of Bristol referred Case VII., the patient having come under his care by reason of an ear infection.

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BIBLIOGRAPHY.

Adrian, E.D. and Matthews, B.H.C. J.Physiol. 1934. (81), 440.

Alabastro, A. Sistem.Nerv. 1949. (1), 54.

Alexander, W.S. J.Neurosurg. 1953. (10), 69.

Alvez, G.J. Arg.brasil.Neuro-psiquiat. 1939. (22), 11.

Anderson, H.A. Yale J.Biol.and Med. 1945. (18), 103.

André, M.J. and Hermans, R. Acta Psych.et Neurol. Belg. 1951. (51), 452.

Angrisani. Osp.psichiat. 1940. (8), 311.

Appelmans, M. Arch.Ophtal. 1935. (52), 835.

Arendt, A. Dtsch.Gesundheitswes. 1953. (8), 137.

Astwazaturov, M. Neurol. Zbl. 1911. p.363.

Aynsley, T.R. Brit.J.Child Dis. 1928. (25), 197.
Brit.J.Ophth. 1929. (13), 612.

Babonniex, J. Huturiel and Widiez. Bull.Soc.Pediatr. 1930. (25), 263.

Baldauf, L.K. J.Med.Res. 1906. (10), 335.

Ballantyne, A.J. Brit.J.Ophthal. 1930. (14), 481.

Ballantyne, A.J. Brit.J.Ophthal. 1940. (24), 65.

Bannister, R.T. St.Barts Hosp.J. 1921. (5), 20.

Barrière, L.A. Perez Fontana V. Mem.Soc.urug.Oftal. 1941. (42), 59.

Baruk, H. Encephale. 1931. (26), 42.

Bates, R. Lancet. 1937. (i), 1282.

Beadles, C.F. Arch.Neurol. 1899. (1), 440.

Bebin, J. Rev.neuro-psiquiat. 1944. (7), 432.

Beck, C.S. Ann.Surg. 1935. (102), 801.

Beltman, J. Arch.Ophthal. 1904. (9), 502.

Bentsen, K.G., Dalsgaard-Nielsen and Möller, H.U. Acta.Ophthal. 1938. (16), 279.

Bentzen, O. Nord.Med. 1947. (33), 465.

Bergstrand, H. Acta.path.microb.scand. 1936. (89), 95 and Supplementum 26.

Bergstrand, H., Olivecrona, H., and Tonnis, W. Gefässmissbildungen und Gefässgeschwulste des Gehirns. Leipzig.

Bethoux, L. Ismel, R. and Marcoulides, J. Rev.neurol. 1936. (66), 611.

Bethoux, L. Ismel, R. and Marcoulides, J. Rev.neurol. 1937. (66), 611.

Bielawski, J.G. and Tatelman, M. Am.J.Roentgen. 1949. (62), 247.

Bluefarb, S.M. Arch.Dermatol. & Syph. 1949. (59), 531.

Blum, J.D. and Mutrux, S. Ophthalmologica. 1949. (118), 781.

Bock, R.H. Amer.J.Ophthal. 1950. (33), 1121.

v.Bogaert, L. Rev.neurol. 1935. (63), 353.

v.Bogaert, L. Acta neurol.psychiat.belg. 1950. (50), 525.

Bonnet, P. Bull.Soc.ophthal.France. 1949. p.828.

Boros. Klin.Mbl.Augenheilk. 1941. (106), 499.

Bouwer, H. van der Heve, and W.Mahoney. Kongl.Akad.Wet.Verhand. 1937. (36).

Bravo, T. and Loayza, F. Rev.neuro-psiquiat. 1943. (6), 317.

Broager, B. and Hertz, H. Acta.psychiat.neurol. scand. 1949. (24), 1.

Brock, S. and Dyke, C.G. Bull.neurol.Inst.N.Y. 1932. (2), 247.

Brushfield, T. and Wyatt, W. Brit.J.Child.Dis. 1927. (24), 98 and 2094.
ibid. 1928 (25), 96.

Burrows, N.F.E. Proc.Roy.Soc.Med. 1947. (40), 9.

Butterworth, T. Arch.Derm.and Syph. 1937. (35), 1159.

Cabannes, C. Arch.ophthal. 1909. (29), 368.

Cairns, H. Lancet. 1951, (ii), 411.

Camp, J.D. Am.J.Roentgen. 1930. (23), 615.

Camp, J.D. J.Amer.med.Ass. 1948. (137), 1023.

Cajano, A. Haematologica. 1948. (32), 359.

Cargnello. Amn.Osp.psichiat. Teramo. 1948. (4), 71.

Casero, L. Arch.Soc.oftal.hisp.Amer. 1946. (6), 370.

Cassirer, R. and Muhsam, R. Berl.Klin.Woch. 1911. (48), 755.
Neurol. Zbl. 1902. (21), 32.

Castonia, G. and Alliani, E. Riv.sper.Freniatria 1955. (79), 661.

Cave-Bondi, Cervello. 1942 (21), 94.

Cavel, L. 1931, These de Paris.

Charamis, J.S. Rev.oto.neuro.ophthal. 1934. (12), 755.

Chiro, G. and Lindgren, E. Acta radiol. 1951. (35), 387.

Clark, J.J. and Tankesley, R.M. J.med.Ass.Georgia. 1951. (40), 99.

Clausen, Klin.Mbl.Augenheilk. 1926. (81), 393.

Cobb, Stanley. Ann.Surg. 1915. (ii). (64).

Cocito, E. Rass.Stud.psichiat. 1951. (40), 379.

Cohen, H.J. and Kay, M.N. Am.J.Dis.Child. 1941. (62), 606.

Conway, M. and Docktor, J.P. Surg.Gynec.Obst. 1947. (84), 866.

Corbin, B., Castellanos, M., Beguez, C. and Fonseca. Rev.med.quir.Oriente. 1944. (5), 234.

Cordero, Atti.Soc.oftal.Ital. 1943. (8), 267.

Cornil, G. Paillas, J.E. and Gastaut, H. Ann.Med.Psych. 1949. (107), 474.

Corradini, E.W. and Browder, E.J. J.Neuropath. 1948. (7), 299.

Correa-Meyer, Arg.Rio-Grande Med. 1941. (20), 275.

Craig, J.M. J.Neuropath. 1949. (8), 305.

Cronzon, O., Christophe, J., Sanchez, M. Rev.neurol. 1933. (40), 361.

Cuperus, Klin.Mbl.Augenheilk. 1909. (47), 334.

Cushing, H. J.Amer.med.Ass. 1906. (47), 178.

Danis, P. and v.Bogaert, L. Acta.neurol.belg. 1951. (51), 74.

Dazzi, L. Riforma med. 1950. (64), 729.

Dechaume, J. and Levy. Lyon.med. 1933. (152), 308.

Delay, J. and Pichot, P. Rev.neurol. 1946. (78), 132.

Del Valle y Adoro, R. Rev.clin.espan. 1955. (57), 38.

Della Torre. 1934 Riv.neurol. 281.

Desana, G. Note Riv.psichiat. 1941. (70), 5.

Dimitri, V. Rev.Asoc.med.arg. 1923. (36), 1029.

Dimitri, V. Rev.Asoc.med.arg. 1936. (50), 1926.

Dimitri, V. and Balado, H. Rev.Asoc.med.arg. 1933. (47), 3045.

Dittrich, J.K. Arch.Kinderheilk. 1953. (146), 151.

Divry, P. and v.Bogaert, L. J.Neurol.Psychiat. 1946. (9), 41.

Dockx, L. Arch.belg.Derm.Syph. 1956. (12), 314.

Donner, M. Acta psych.neurol.scand. 1953. (28), 269.

Downing, D.F. and Kreidberg, M.B. J.Pediat. 1949. (34), 564.

Dufourmental, L. Bull.Soc.Chirurg. Paris. 1936. (28), 103.

Duhamel, E. and Goetz, G. Bull.Soc.Ophthal. France. 1954. (6), 541.

Dürck, H. Atti.del I Congresso Rutemaz di Patol.Torino. 1911.

Eaves, E.C. Brain, 1926. (49), 307.

Eckel, K. Wien.Z.Nervenheilk. 1950. (3), 184.

Ellis, R.W.B. Proc.R.Soc.Med. 1932. (25), 954.

Ellis, R.W.B. Proc.R.Soc.Med. 1946. (39), 135.

Elschnig, A. Z.Augenheilk. 1918. (39), 189.

Engelhardt, H. Psych.neurol.Woch. 1942. (44), 313.

Erbsen. Verh.dtsch.roentg.Gesell. 1938. (58), 141.

Esser, P. Arch.Psych.Nervenkr. 1941. (113), 440.

Floris, V. Vizioli, R. Riv.Neurol. 1952. (22), 711.

Fracasso, L. Riv.Neurol. 1946. (16), 447.

Fracasso, L. Arch.Psicol.Neurol.Psichiat. 1948. (9), 1.

Freese. Kl.Mbl.Augenheilk. 1920. (65), 922.

Frigyer, L. Arch.Psychiat.Neurol. 1930. (3), 5.

Fuentes, Z. Rev.chil.Pediat. 1955. (26), 8.

Furtado, D. Rev.neurol. 1936. (65), 640.

Gammel, J.A. Arch.Derm.& Syph. 1936. (34), 698.

Halezowski, M. Ann.Dermatol.Syph. 1898. (9), 242.

Geyelin, H.R. and Penfield, W. Arch.Neurol. & Psychiat. Chicago. 1929. (2), 1020.

Giampalmo, A. Pathologica. 1940. (32), 192.

Ginzburg, J. Klin.Mbl.Augenheilk. 1926. (76), 393,

de Gispert-Cruz, I. Rev.clin.espan. 1942. (4), 233.

Goeters, W. Mschr. Kinderheilk. 1941. (86), 122.

Goldberg, S. Arch.Dermatol.Syph. 1946. (53), 503.

Gotze, W. Zbl.Neurochir. 1953. (13), 41.

Granström, K.O. Acta.ophthal. 1935. (13), 115.

Graul, E. Hautarzt. 1953. (4), 510.

Green, J.F. Amer.J.Roentg. 1950. (64), 391.

Green, J.R. J.Neuropath. 1945. (4), 27.

Green, J.R., Foster, J. and Berens, D.L.
Amer.J.Roentg. 1950. (64), 391.

Greenwald, H.M. and Koota, J. Am.J.Dis.Child.
1936. (51), 868.

Greig, D.M. Edin.med.J. 1922. (28), 105.

Haemmerlinck, C., Myle, G., and v.Bogaert, L.
J.Neurol.Psychiat. 1947. (10), 93.

Haines, J.W. and Pumphrey, G.H. Am.J.Dis.Child.
1941. (61), 557.

Hanes, F.M. J.exp.Med. 1912. (16), 512.

Hebold, O. Arch.Psychiat.Nervenkr. 1913. (51),
445.

Henblein, G.W., Pendergass, E.P. and Widmann, B.P.
Radiol. 1940. (35), 701.

Hoehne. Z.Augenheilk. 1937. (93), 105.

van der Hoeve, J. Ber.Versamm.deutsh.ophthal.Ges.
1936. (51), 136.

van der Hoeven, L.H. Nederl.Tydschr.Geneesh.
1950. (94). 141.
Zbl.Neurol. 1951. (112), 247.

Horrocks, P. Trans.Ophthal.Soc.U.K. 1883. (3),
106.

Hosoi, K. Am.J.Path. 1930. (6), 235.

Huber, K. and Zweymüller, E. Wien.Z.Nervenheilk.
1954. (9), 459.

Hudelo, A. Ann.Oculist. 1929. (166), 889.

Hugo, H.J. J.med.Ass. S.Africa. 1927. (1), 534.

Iannuccelli, C. Riv.sper.Freniat. 1949. (73), 399.

Ironside, R. & Hill, D. J.ment.Sc. 1941. (87), 631.

Isenschmidt, R. Munch.med.Woch. 1912. 59, (i), 243.

Jardezki, A.S. Zbl.ges.Ophthal. 1939. (43), 166.

Jervis, G. J.Neuropath. 1954. (13), 318.

Joiris, P. et Fanchamps, J. Bull.Soc.belg.Ophthal. 1935. (70), 92.

Jørgensen, J. Nord.Med. 1943. (17), 126.

Joy, H.H. Trans.Amer.Ophthal.Soc. 1949. (47), 93.

Juba, A., Sjandtner, G. and Zeteny, G. Orvosi hetilap. 1955. (96), 329.

Juba, A., Zeteny, G. Mschr. Psychiat. 1956. (131), 163.

Kadyi. Klin.Mbl.Augenheilk. 1930. (84), 866.

Kalischer, S. Berlin Klin.Woch. 1897. (4), 1059.
Arch.Psych. 1901. (34), 171.

Kammer, G. Z.menschl.Vererb. 1955. (33), 203.

Kan, O. and Takahashi, K. Psych.Neurol.jap. 1940. (44), 56.

Kantorek, R. Casop.lek.cesk. 1940. (79), 314.

Kasanin, J. and Krank, R.P. Arch.Neurol.Psychiat. Chicago. 1935. (34), 164.

Kautzky, R. Dtsch.Z.Nervenheilk. 1949. (161), 506.

Kautzky, R., Wohlter, R. Z.Nervenheilk. 1952. (168), 24.

Kavka, H. and Holisova, L. Cesk.ofthal. 1953. (9), 527.

King, G. and Schwarz, G.A. Arch.int.Med. 1954. (94), 743.

Kiranoff. Klin.Mbl.Augenheilk. 1925. (74), 502.

Kissel, P. and Arnould, G. Rev.neurol. 1954. (91), 381.

Kleyntjens, F. Acta neurol.psychiat.belg. 1948. (48), 111.

Kluska, V. Spisy.lek.Fak.Masaryk.Univ. 1947. (20), 173; 285.

Knapp, A. Trans.Amer.Ophthal.Soc. 1927. (25), 154.

Koch, G. Z.ges.Neurol.& Psychiat. 1940. (168), 614.

Koch, G. Arztl. Forsch. 1949. (3), 551.
ibid 1950. (4), 625.

Koessler,-. Bull.Soc.Radiol.med. 1933. (21), 671.

Kohler, -. Zbl.Pathol. 1940. (75), 81.

Komoto, -. Klin.Mbl.Augenheilk. 1922. (69), 158.

Kostonlas, A. Ann.Oculist.Paris. 1932. (169), 341.

Krabbe, K.H. Arch.Neurol.Psych.Chicago. 1934. (32), 737. Rev.neurol. 1955. (93), 199.

Krabbe, K.H. and Wissing, O. Acta radiol. 1929. (10), 523. Revue.neurol. 1932. (39), 394.

Krause, K. Z.Augenheilk. 1929. (68), 244.

Kroll, F.W. and Staemmler, M. Arch.Psychiat. 1948. (181), 168.

Kufs, H. Z.ges.Neurol.& Psychiat. 1928. (113), 651.

Kühnke,F. Mschr.Kinderheilk. 1941. (88), 78.

Kylin, E. and Kjellin, T. Acta med.scand. 1936. (88), 1708.

Lachmann, F. Radiol. 1936. (27), 75.

Laignel-Lavastine, Delherm and Fouquet, J. Revue neurol. 1929. (36), 475.

Langs, A., Waeckel, C., Brann, J.P. J.franc Radiol.Elect.Med. 1955. (36), 204.

Lannois and Bernoud. Nouv.Iconog.Salpet. 1898. (11), 446.

Lasierra, P.A., Sanchez-Arroyo, J. Rev.clin.espan. 1955. (56), 382.

Lawford, J.B. Trans.ophthal.Soc.U.K. 1885. (5), 136.

Lennox, W.G., Gibbs, F.A. and Gibbs, E.L. Arch.Neurol.& Psychiat. Chicago. 1936. (36), 1236.

Levison, H. Acta psychiat.neurol.scand. 1955. (30), 257.

Levy, G. Presse med. 1930. (38), 37.

Lichtenstein, B.W. and Lev, M. Arch.Neurol.& Psychiat. Chicago. 1943. (49), 507.

Lichtenstein, B.W. Arch.Neurol.& Psychiat. 1954. (71), 291.

Lichtenstein, B.W. and Rosenberg, C. J.Neuropath. 1947. (6), 369.

Lindgren, E. Nervenarzt. 1939. (12), 138.

Livingston, S., Eisner, V., Brown, W.H. and Boks, L. Post-grad.Med. 1956. (19), 221.

Lomholt, M. Ugesk.Laeger. 1941. (103), 613.

Longo, G. Arch.Radiol. 1949. (23), 99.

Louis-Bar, D. Confinia neurolog. 1944. (6), 1.

Louis-Bar, D. Acta neurol.psych.belg. 1950 (50), 525.

Luengo, J.E. and Rey, G. Actas dermo.sif. 1945. (36), 825.

Lund, M. Acta psychiat. neurol.scand. 1949. (24), 569.

Luschka, H. Virch. Arch. 1854. (6), 458.

de Magalhaes, C.W. Arch.brasil Med. 1945 (35), 343.

Mallory, F.B. J.Path.Bact. 1896. (3), 110.

Mannelidis, E.E. Arch.Psychiat. 1950. (184), 601.

Manolesco, D., Lazaresco and Vintilesco, D. Rev.d'Oto-neuro-ophth. 1938. (16), 664.

Marchesani, O. Wien.med.Woch. 1925. (75), 2538.

Marcos, J.R., Pacheco Olivera, M. Arch.Pediat. Urug. 1953. (24), 125.

Marque, A.M. Rev.Oto-neuro-oftal. 1927. (1), 202.

Marques, A. Rev.neurol.B.Aires. 1945. (10), 256.

Marsal, J. and de Gispert Cruz, I. Actas dermo.sif. 1944. (35), 404.

Medlicott, R.W. N.Z. med.J. 1945. (44), 143.

Meignant, P., and Baudoin, D. L'Angiomatose Encephalo-trigeminée. Paris. G.Doin. 1947.

Mettler, F.A. J.Neuropath. 1947. (6), 98.

Meyer, F. Mbl.Psychiat.Neurol. 1936. (92), 294.

Meyer, J.E. Arch.Psychiat. 1951. (186). 437.

Mezner, T. Budapest Orvos.Ujsag. 1938. (36), 506.

Milles, W.J. Trans.ophthal.Soc.U.K. 1884. (4), 168.

Molinari, -. Riforma med. 1940. (56), 1036.

Møller, H.U. Z.ges. ophthal. 1938. (41), 614.

Moniz, E. and Lima, A. Rev.neurol. 1935. (63), 743.

Monnier, M. and Mutrux, S. Schweiz.Arch.Neurol. Psych. 1950. (66), 417.

Moore, R.F. Brit.J.Ophthal. 1929. (13), 252.

Moreno, G. Minerva Nipiolog. 1953. (3), 301.

de Morsier, G. and Franchescatti, A. Schweiz.med. Woch. 1937. (67), 285.

Mouriquand and Bernheim. Lyon Med. 1924. (83), 49.

Muller, H.H. Mschf. Psychiat. 1923. (53), 243.

Muscettola, G. Radiol.med. 1947. (33), 534.

Myle, G. and Lowenthal, A. Acta neurol.psychiat. belg. 1950. (50), 473.

Myle, G. and Tytgat, H.A. J.belg.Neurol.Psychiat. 1943. (56), 250.

Mylius, K. Klin.Mbl.Augenheilk. 1930. (85), 303.

McCoy, A.D., and Voris, H.C. Arch.Neurol.Psych. Chicago. 1948. (59), 504.

McKernan, R.L. Trans.ophthal.Soc.U.K. 1946. (66), 683.

McMahon, R.J. Arch.Otolaryng. 1951. (54), 542.

Näcke, P. Neurolog.Zbl. 1905. (24), 930.

Nakamura, B. Klin.Mbl.Augenheilk. 1922. (69), 312.

Neder, J.E. Ann.Congr.Inter-Amer.Med. 1946. (1), 601.

Neimann, N., Pierson, M. and Manciaux, M. Rev.med.Nancy. 1953. (78), 353.

Newson, A.L. Brit.med.J. 1939, (ii). 1088.

Nussey, A.M. and Miller, H.H. Brit.Med.J. 1939, (i), 822.

O'Brien, C.S., and Porter, C.W., Arch.Ophthal. 1933. (9), 715.

Ohno, T. Jap.J.Dermatol. 1929. (29), 417.

Oppenheim, H. Neurol.Zbl. 1913. (32), 1.

Paarman, H.F. Dtsch.Z.Nervenheilk. 1955. (173),21.

Paarnitzke, K.H. Zbl.Neurochir. 1956. (16), 92.

Padovani, S. Atti.Congr.Soc.oftal.ital. 1935. 689.

Paillas, J., Guillot and Gallian. Marseille Méd. 1943. (31), 496.

Panara, L. Riv.Neurolog. 1934. (7), 579.

Paton, L. and Collins, E.T. Trans.ophth.Soc.U.K. 1919. (39), 157.

Paunessa, J.M., Bellouard, F. and Cremona, A.C. Arch.oftal.B.Aires. 1949. (24), 257.

Péhu, M., Dechaume, J. and Boucoumont, J. Lyon med. 1932. (149), 249.

Penfield, W. and Ward, A.A. Arch.Neurol.& Psych. Chicago. 1948. (60), 20.

Perosio, A.M., Burucua, J.E., Kaplan, S., and Dubra, C.C. Prensa med.argent. 1953. (40), 1848.

Persichetti. Bull.Oculist. 1941. (20), 133.

Peters, G. Z.ges.Neurol. 1939. (164), 365.

Peters, G. Z.ges.Neurol. 1939. (164), 365.

Peters, G. and Tebelis, F. Z.ges.Neurol. 1937. (157), 782.

Philips, F. Pathol.Infant. 1931. (5), 1.

Pilcher, C. Ann.Surg. 1946. (123), 766.

Pilcher, C., Meacham, W.F. and Cobb, C.A. Surgery. 1950. (28), 342.

Pinto-Pupo, P. Arq.neuro-psiquiat. 1953. (11), 209.

Popp-Vogt, C. Arch.franc.Paediat. 1951. (8), 50.

Radermecker, J. Acta.neurolog.psychiat.belg. 1951. (51), 427.

Rawlings, L.B. Proc.Roy.Soc.Med. 1928. (22), 442.

Rigola, A. Riv.sper.Freniat. 1953. (77), 5.

Riser,,R.O. Amer.J.Ophthal. 1936. (19), 155.

Rocca, E.D. and Franco, J. Rev.neuro-psiquiat. 1947. (10), 379.

Rocke, J.M. Proc.Roy.Soc.Med. 1932. (25), 793.

Rodigina, A.M. Arch.Ophthal. 1944. (32), 214.

Rodriguez, B., and Canbarrère, N.L. Ann.Fac.Med. Montevideo. 1950. (35), 1061.

Roederer, J., Lobstein, A., and Philipides, D. Bull.Soc.franc.Derm.Syph. 1952. (59), 486.

Rogers, L. Brit.J.Surg. 1933. (21), 229.

Rønne, H. Acta derm.venereol. 1937. (18), 591.

Rørvik, K. Nord.Med. 1947. (34), 1104.

v.Rötth, A.
(1) Z.ges.Ophthal. 1929. (20), 588.
(2) Klin.Mschr.Augenheilk. 1928. (80), 405.

Rullan, P.J., and Rifkinson, N. Bol.Asoc.med. Puerto Rico. 1954. (46), 108.

Sachs, E. J.Neurosurg. 1948. (5), 354.

Sachs, E. Amer.J.med.Sc. 1915. (150), 565.

Safar, K. Klin.Mbl.Augenheilk. 1923. (51), 301.

Salus, R. Klin.Mbl.Augenheilk. 1923. (71), 305.

Sato, S. Acta Soc.ophthal.jap. 1941. (45), 142.

Schaefer, W. Mschfr. Kinderheilk. 1931. (50), 35.

Schaub, C.F. Amer.J.ophthal. 1940. (23), 813.

Scheinker, I. Zbl.Neurol. 1938. (163), 604.

Schenk, V.W.D. Psych.neurol.Blad. 1940. (14), 32.

Schiøtz, E.H. Acta.psych.neurol. 1935. (10), 683.

Schiøtz, E.H. Norsk Mag. Laeg. 1935. (96), 737.

Schmidt, G. Nervenarzt. 1952. (23), 310.

Schondel and Laursen. Hospitalstid. 1936: 489.

Schirmer, R.S. Archiv.Ophthal. 1860. (7), 119.

Schuller, -. Zbl. Hautkr. 1931. (35), 601.

Servelle, M. Presse med. 1945. (53), 353.

Shafar, J. Glasgow med.J. 1946. (27), 109.

Skydsgaard, K. Acta.ophthal. 1935. (13), 273.

Snellman, A. Acta.Soc.medd.Fenn. 1945.(34), 1.

Soejoenses, R.M. Geneesk.Tijdsch.Neder.Ind. 1941. (81), 2650.

Sole-Sagarra, F. Z.Kinderpsych. 1954, (21), 65.

Sommer, F. Fortschfr.Geb.Roentgen. 1950. (73), 581.

Sommer, F., and Demoullin, M. Paris med. 1947. (37), 560.

Souques, Alajouanine and Mathieu. Rev.neurol. 1921. (28), 1127.

Spatz, H. Z.ges.Neurol. 1922. (77), 261.

Spiguel, D. Rev.neurol.B.Aires. 1941. (6), 50.

Spiller, W.G. Arch.Neurol.Psychiat. Chicago. 1919. (2), 50.

Steffens. Klin.Mbl.Augenheilk. 1902. (40), 113.

Steliana. "Contribution à l'Étude de la Maladie de Sturge-Weber". 1939. Thèse. Bucharest.

Stewart, R.M. and Ashby, W.R. J.Neurol. and Psychopath. 1931. (11), 289.

Stoewer, P. Klin.Mbl.Augenheilk. 1908. (46), 323.

Stokes, J.J. South.med.J. 1957. (50), 82.

Strang, C. Edin.med.J. 1949. (56), 409.

Streeter, G.L. Contributions to Embryology. (Carnegie Institution, Washington), 1918. (8), 5.

Ströbel, H. Arch.Derm.Syph. 1943. (183), 468.

Strominger, L. Spitalul (rum). 1905. (25), 147.

Sturge, W.A. Trans.clin.Soc.London. 1879. (12), 162.

Subirana, A. 1933 "Los sindromes vasc. neurocutaneos". Madrid.

Subirana and Carulla, V. Rev.neurol. 1933. (11), 1195.

Suglian, V. Klin.Mbl.Augenheilk. 1929. (83), 825.

Suryaninoff, B. Ugesk.Laeger. 1943. (105), 683.

Terrana, V. Acta.neurol. 1948. (3), 477.

Thayer, W.H. Northwest Med. 1956. (55), 304.

Tietze. Zbl.Chir. 1920. (20), 401.

Tingey, A.H. J.ment.Sc. 1956. (102), 178.

Touraine, A., Gole, L. and Sambron, J. Bull.Soc.franç.derm.Syph. 1936. (43), 618.

Touraine, A., Solente, and Piquart, A. Bull.Soc.franç.Derm.Syph. 1936. (43), 1810.

Touraine, M.A., Ann.Derm.Syph. 1943, p.94.

Tramer, M. Schweiz.med.Woch. 1943. (73), (i)., 44.

Tyson, H.H. Arch.Ophthal. 1932. (8), 365.

Uiberall, H. Z.ges.Neurol. 1930. (124), 863.

Ulutin, O.N., and Kumuru, S. Turk.med.J. 1956. (22), 417.

Valenciano, L., and Inchaurrandietta, P.M. Rev.espan.Neuro-oftal. 1947. (6), 377.

Vampre, E., and Villaca. Rev.Cir.Sao Paolo. 1938. (4), 3.

Vannas, -. Finska Lak.Kap. 1934. (76), 399.

Vanzetti, -. Arch.Biol.Patol. 1894. (58).

Verbeek, F. Psychiat.neurol.Blad. 1937. (41), 118.

Vincent, C. and Heuyer, G. Rev.neurol. 1929. (36), 509.

Vizioli, R. and Floris, V. Riv.neurol. 1953, (23), 383.

Vogele. Klin.Mbl.Augenheilk. 1928. (81), 393.

Volland, R. Z.Erforsch.Behand.jug.Schwachsinn. 1912. (6), 130.

Volland, -. Roentgenpraxis. 1930. (2), 619.

Wachsmuth, N. and Lowenthal, A. Acta.neurol. psychiat.belg. 1950. (50), 305.

Wagenmann, A. Archiv.Ophthal. 1900. (51), 532.

Weber, F.P. J.Neurol.& Psychopath. 1922. (3), 134. Proc.Roy.Soc.Med. 1929. (22), 431.

Weber, F.Parkes. Brit.med.J. 1936. (708).

Weber, F.Parkes. "Rare Diseases and Some Debatable Subjects". London. Staples Press. 1946.

Welikala, A.H.N. Brit.J.Radiol. 1952. (25), 55.

Widerhold, A., Neira, M., Nazer, J., Rev.chil. Pediat. 1956. (27). 70.

Wiesner, E. Österr.Z.Kinderheilk. 1953. (9), 247.

Wilson, S.M. Proc.Roy.Soc.Med. 1957. (50), 107.

Wiswell, G.B., Marshall, C.S. and Metcalfe, D.C. Canad.med.Ass.J. 1949. (61), 623.

Wohlwill, F.J., and Yakovliev, P.I. J.Neuropath. 1957. (16), 341.

Woringer, E., and Baumgartner, J. Rev.Otoneurol. 1954. (26), 238.

Worster-Drought, C. Brit.med.J. 1948, (ii); 414.

Wyburn-Mason, R. "Vascular Abnormalities and Tumours of the Spinal Cord". London. Kimpton 1943.

Yakovlief, P.I., and Guthrie, R.H. Arch.Neurol. Psychiat. Chicago. 1931. (26), 1145.

Yamanaka, T. Klin.Mbl.Augenheilk. 1927. (78), 372.

Zaun, W. Klin.Mschr. Augenheilk. 1924. (72), 57.

Zavalia, A. Ophthal.ibero-amer. 1947. (8), 363.

Zvereva, -. Zbl.ges.Ophthal. 1929. (29), 847.